FLUENSULFONE (265)

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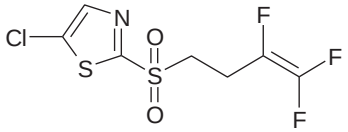
EXPLANATION

Fluensulfone is a non-fumigant, fluoroalkenyl nematicide used to control nematode pests in cucurbit vegetables, eggplant, peppers, and tomatoes. Fluensulfone shows activity in multiple nematode physiological systems; however, its specific nematicidal activity is not known at this time. Fluensulfone was considered for the first time for toxicology by the 2013 JMPR and for residues by the 2014 JMPR.

IDENTITY

ISO common name	Fluensulfone (provisionally approved)
Chemical Name	
IUPAC	5-chloro-1,3-thiazol-2-yl 3,4,4-trifluorobut-3-en-1-yl sulfone
CAS	5-chloro-2-[(3,4,4-trifluoro-3-buten-1-yl)sulfonyl]thiazole
CIPAC No.	Not Listed
CAS No.	318290-98-1
Synonyms	MCW-2
Structural Formula	
Molecular formula	$C_7H_5ClF_3NO_2S_2$
Molecular mass	291.7

Physical and chemical properties

Physical and chemical properties of fluensulfone

Property	Guideline and method	Test material specification and purity	Findings	Reference
Technical Grade Active Ingredient				
Melting point (Technical material)	EEC A1 OECD 102 OPPTS 830.7200	Batch No.: 36372130-291-PF1 96.75%	Mean of two determinations by DSC: 34.8 °C ± 0.5 °C (308.0 K ± 0.5 K)	Weissenfeld M., 2009 R-23310A
Boiling point (Technical material)	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 36372130-291-PF1 96.75%	No boiling point determined by DSC, as material decomposed without boiling. Atm. pressure = 99.6 kPa	Weissenfeld M., 2009a R-23310A
Decomposition temperature (Technical material)	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 36372130-291-PF1 96.75%	The test substance begins to decompose without boiling at 215 °C (capillary method). Atm. pressure = 99.6 kPa	Weissenfeld M., 2009a R-23310A

Property	Guideline and method	Test material specification and purity	Findings	Reference
Physical state and colour	OPPTS 830.6302 OPPTS 830.6303	Batch No.: 36372130-291-PF1 96.75%	Yellow, resin like solid.	Weissenfeld M., 2010 R-23307
Odour	OPPTS 830.6304	Batch No.: 36372130-291-PF1 96.75%	"Specific odour"	Weissenfeld M., 2010 R-23307
Solubility in organic solvents	EEC A6 OECD 105	Batch No.: 36372130-291-PF1 96.75%	Solubilities at 20 °C (shake flask method): Acetone 350.49 g/L Dichloromethane 306.14 g/L Ethyl acetate 350.76 g/L n-Heptane 19.01 g/L Methanol 359.29 g/L n-Octanol 90.42 g/L Xylene 356.18 g/L	Weissenfeld M., 2009d R-23317
Hydrolysis rate at pH 4, 7 and 9	OPPTS 835.2120 OECD Guideline 111.	[thiazole-4-^{14}C]fluensulfone Radiochemical Purity 97.2%	After 5 days at 50 °C and pH 4, 5 and 7, the concentration of [thiazole-^{14}C]fluensulfone comprised ≥ 96.8% of the applied dose in all samples.	Shepler, K 2010 R-23319
Pure Active Ingredient				
Melting, freezing or solidification point	EEC A1 OECD 102 OPPTS 830.7200	Batch No.: 381-022-02 99.1%	Mean of two determinations by DSC: 34.4 °C ± 0.2 °C (307.6 K ± 0.2 K)	Weissenfeld M., 2008a. R-23309
Boiling point	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 381-022-02 99.1%	Mean of two determinations by DSC: 282.5 °C ± 0.2 °C (555.7 K ± 0.2 K) Atm. pressure = 100.2 kPa	Weissenfeld M., 2008b R-23310
Temperature at which decomposition or sublimation occurs	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 381-022-02 99.1%	No decomposition or sublimation observed. Boiling point successfully determined.	Weissenfeld M., 2009a R-23310A
Relative density of purified active substance	EEC A3 OECD 109 OPPTS 830.7300	Batch No.: 381-022-02 99.1%	Relative density at 20 °C = 1.876 (Gas comparison pycnometer)	Weissenfeld M., 2008c R-23312
Vapour pressure of purified active substance	EEC A4 OECD 104	Batch No.: 381-022-02 99.1%	Vapour pressure results: 25 °C = 3.0×10^{-2} Pa 35 °C = 1.3×10^{-1} Pa 45 °C = 3.4×10^{-1} Pa (Gas saturation method) Vapour pressure extrapolated from vapour pressure curve was calculated to be 3.0×10^{-2} Pa at 25 °C	Weissenfeld M., 2008d R-23313
Henry's Law constant	Calculation	Batch No.: 381-022-02 99.1%	1.68×10^{-2} Pa m^3/mol	Weissenfeld M., 2009b R-23313A
Physical state and colour	OPPTS 830.6302 OPPTS 830.6303	Batch No.: 381-022-02 99.1%	White, fine crystalline powder	Weissenfeld M., 2010 R-23307

Property	Guideline and method	Test material specification and purity	Findings	Reference
Odour	OPPTS 830.6304	Batch No.: 381-022-02 99.1%	"Specific odour"	Weissenfeld M., 2010 R-23307
Solubility in water	EEC A6 OECD 105 OPPTS 830.7840	Batch No.: 381-022-02 99.1%	Water solubility at 20 °C = 545.3 mg/L (shake flask method)	Weissenfeld M., 2008e R-23316
n-octanol/water partition coefficient	EEC A8 OECD 117 OPPTS 830.7570	Batch No.: 381-022-02 99.1%	Log P_{ow} = 1.96 (HPLC method)	Weissenfeld M., 2008f R-23318
	Based on solubilities	Not Applicable	Log P_{ow} based on individual solubilities in n-octanol and water: n-Octanol solubility: 90.42 g/L Water solubility: 0.545 g/L Log P_{ow} = Log (90.42/0.545) = 2.2	
Direct phototransformation of purified active substance in water	OPPTS 835.2240 OECD Proposal for a New Guideline Phototransformation of Chemicals in Water (2007)	[thiazole-4-^{14}C]fluensulfone trifluorobutene-1,2-^{14}C]fluensulfone	Aqueous photolysis may contribute to the rapid degradation of fluensulfone in the environment. DT_{50} irr. = < 11 hours of continuous sun test irradiation, when extrapolated to environmental conditions results in a DT_{50} < 1 day for all latitudes.	Schick, M 2011 R-23322

Fluensulfone is registered as an emulsifiable concentrate (EC) formulation containing 480 g ai/L.

METABOLISM AND ENVIRONMENTAL FATE

Metabolism and environmental fate studies were conducted with [thiazole-4-^{14}C]fluensulfone and [trifluorobutene-1.2-^{14}C]fluensulfone (Figures 1 and 2).

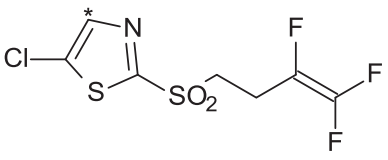


Figure 1 [thiazole-4-^{14}C]fluensulfone

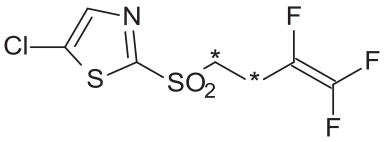
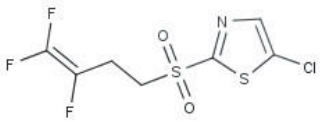
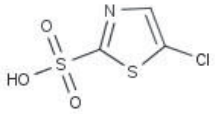
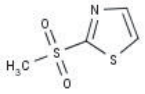
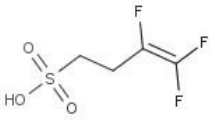
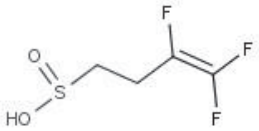
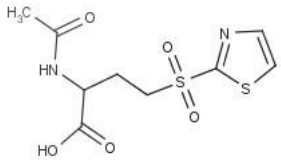
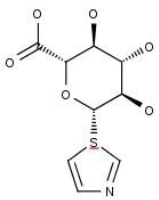


Figure 2 [trifluorobutene-1,2-^{14}C]fluensulfone

Chemical names, structures, and code names of metabolites and degradation products of fluensulfone are shown below.

Known metabolites and degradation products of fluensulfone

Code Names	Chemical name, molecular formula, molar mass	Structure	Where found
Fluensulfone (parent compound) MCW-2	CAS: 5-chloro-2-(3,4,4-trifluoro-but-3-ene-1-sulfonyl)-thiazole CAS No. 318290-98-1 IUPAC: 5-chloro-1,3-thiazol-2-yl 3,4,4-trifluorobut-3-en-1-yl sulfone $C_7H_5ClF_3NO_2S_2$ 291.70 g/mol		Soil, poultry, rotational crops (minor)
M-3625 Thiazole sulfonic acid TSA	IUPAC: 5-chloro-1,3-thiazole-2-sulfonic acid $C_3H_2ClNO_3S_2$ 199.64 g/mol		Soil, crops, rotational crops, rat (minor)
M-3626 Thiazole methyl sulfone MeS	IUPAC: 2-methylsulfonyl-1,3-thiazole $C_4H_5NO_2S_2$ 163.22 g/mol		Soil, ruminant, rat (minor)
M-3627 Butene sulfonic acid BSA	IUPAC: 3,4,4-trifluorobut-3-ene-1-sulfonic acid $C_4H_5F_3O_3S$ 190.14 g/mol		Soil, crops, rotational crops, rat (minor)
Butene sulfinic acid	IUPAC: 3,4,4-trifluorobut-3-ene-1-sulfinic acid $C_4H_5F_3O_2S$ 174.14 g/mol		Rat, ruminant
thiazole mercapturate	IUPAC: 2-acetamido-4-(1,3-thiazole-2-sulfonyl)butanoic acid $C_9H_{12}N_2O_5S_2$ 292.33		Rat
MW-327-I and MW-327-II Thiazole glucuronides (α and ß isomers)	Structure not specified $C_9H_{12}NO_6S$ 262.26		Rat

Animal Metabolism

The Meeting received metabolism studies on laboratory animals (2013 Meeting), lactating goats, and laying hens. Note that in the tables below, all data are reported to the level of precision specified in the study reports. All of the studies were conducted with fluensulfone which was radio-labelled,

separately, in the thiazole ring [Thiazole-4-^{14}C; Th-^{14}C] and the ethane bridge between the sulfonyl and trifluorobutene moieties [Trifluorobutene-1,2-^{14}C; Bu-^{14}C].

In animals, fluensulfone is cleaved at the sulfonyl bridge, apparently via glutathione conjugation, to yield products based on the thiazole and trifluorobutene halves of the parent molecule, with each half having the SO_x moiety. No parent fluensulfone was detected in any rat or lactating goat matrix, whereas parent fluensulfone was a major residue (> 10% of the total radioactive residue, TRR) in poultry fat. In both lactating goat and laying hen, radiolabel from fluensulfone was incorporated into natural products (lactose/glucose in the goat study; sugars, fatty acids, and proteins in the hen study).

Laboratory animals

Fluensulfone was rapidly absorbed at a dose level of 5 mg/kg bw, but the absorption phase was significantly longer at 500 mg/kg bw. The recovery of excreted radiolabel was 94–99% for individual rats. Radiolabel was found mainly in urine (71–83%), faeces (9–11%) and the cage wash (6–16%). One day after dosing with radiolabelled fluensulfone, an average of 0.6–0.8% of the administered radiolabel was in liver and 0.1% in kidney, with 1.7–2.1% in the carcass and 4.5–4.7% remaining in the gastrointestinal tract. By 7 days after treatment with radiolabelled fluensulfone, an average of 0.1–0.2% of the administered radiolabel remained in liver, and 0.03% in kidney.

The majority of the faecal radioactivity was not identified. It consisted of a number of peaks, each representing less than 2% of the administered dose; the only faecal metabolite representing more than 5% of the administered dose was thiazole sulfonic acid. In urine, there were no metabolites common to both radiolabels, which indicate that the initial step is cleavage at the sulfonyl bond. The initial reaction is probably with glutathione to release the trifluorobutene group and conjugation of the thiazole moiety.

Lactating goats

The metabolism of fluensulfone in lactating goats was investigated by LaMar and Quistad (2010, Study R-25458). For each radiolabel position, a single goat was dosed for five days at ca. 29 mg/day (equivalent to 10 ppm in the diet). Milk was collected twice daily and excreta were collected once daily throughout the study. Goats were sacrificed 20–22 hours after the final dosing, at which point tissues, bile, blood, and GI tract (with contents) were collected for analysis.

Total radioactive residues were determined by liquid scintillation counting (LSC) of solubilized tissues (liver, kidney, muscle, blood, bile, and fat), combusted samples (faeces, GI tract), or direct counting (urine). Samples of liver, kidney, and muscle were extracted with twice with acetonitrile:water (ACN:H_2O, 1:1, v/v) and once by ACN (neat) for extraction of residues for characterization and identification. Samples of flank muscle from the butene-label treated goat were additionally extracted with hexane:acetone (4:1, v/v) followed by acetone (neat) prior to alkaline

treatment of the post-extraction solids (PES). Residue analysis for these extracts was by high-performance liquid chromatography (HPLC) and, in some cases, thin-layer chromatography (TLC). For milk, the fat component was separated by centrifugation and extracted with acetone:hexane (1:4, v:v) and then once with acetone. The non-fat milk portion was extracted with acetone to precipitate milk proteins, which were then extracted with acetone:water (1:1, v:v). The resulting extract was added back to the skim milk for direct analysis by HPLC and TLC. Post-extraction solid fractions of all matrices except skim milk and poultry fat underwent further treatment, including alkaline digestion which was followed by acid digestion for liver and kidney (butene label only). Numerous HPLC systems with varying stationary and mobile phases were investigated to achieve satisfactory separation of the radiolabelled components, with detection by UV absorption or mass spectrometry (MS). Identification of metabolites was by co-chromatography with known standards and/or by mass spectral analysis.

The total recovery of radioactivity was 67 and 87% of the AD for the thiazole- and butene-labels, respectively. Low total recovery could be attributed to conversion of radiolabelled material to $^{14}CO_2$ and the fact that the entire carcass was not analysed for radioactivity. Most of the radioactivity was recovered in urine (38–70% of the AD). The thiazole label excretion in urine was only 53% that of the butene label. Faeces and the gastrointestinal tracts, at sacrifice, contained 14–19% of the AD. Radioactivity in tissues and body fluids accounted for 11% (thiazole-radiolabel) and 3.5% (butene-radiolabel) of the administered dose (Table 1). For both radiolabel positions, residues appeared to plateau in skim milk and reach a steady state of excretion by Day 2 or Day 3 (Tables 2 and 3). It is unclear whether or not residues in milk fat reached a plateau during the treatment phase of the study.

The TRR levels were highest in the liver (0.87–1.6% of AD), followed by kidney (0.1–0.2% of AD). TRR levels in thiazole-labelled muscle samples were about 4 times those found in the butene-labelled muscle samples (ca. 0.22–0.24 mg fluensulfone eq/kg vs. ca. 0.04–0.05 mg fluensulfone eq/kg). Muscle contained 4.2% of the AD for the thiazole label and ca. 1% of the AD for the butene label. Fat had low levels of radioactivity (ca. 0.07–0.13 mg fluensulfone eq/kg (thiazole label) and 0.04–0.07 mg fluensulfone eq/kg (butene label)). Milk contained 1.7% (thiazole label) and 1.1% (butene label) of the administered dose with the thiazole label being excreted at a higher rate than the butene label.

Fluensulfone and the known plant metabolites (i.e. methyl sulfone, thiazole sulfonic acid and butene sulfonic acid) were not identified in any of the goat milk or tissue samples. Thiazole methyl sulfone (25% TRR) and butene sulfinic acid (66% TRR) were identified in urine as major metabolites. No other fluensulfone-related ^{14}C-residues could be identified in any other matrix. Major radiolabelled residues were extensively broken down and appeared to be incorporated into natural products.

Lactose and glucose accounted for the majority of the radioactive residues in liver (ca. 8–9% of the TRR). The majority of the radioactivity, extractable by strong alkaline treatment (24% KOH), was assumed to be composed of a range of other sugars and natural products. Lactose was also the

major residue in skim milk (ca. 46–63% of the TRR). The majority of the remaining radioactivity (31–38% of the TRR) in both skim milk and liver was associated with proteins and amino acids. Radiolabelled glucose was also seen in kidney (13–17% of the TRR). Radioactivity associated with proteins in kidney accounted for 25–36% of the TRR.

Incorporation of radiolabelled residues into triglycerides was apparent in all fat matrices. In milk fat, radioactivity associated with fatty acids accounted for 8 and 31% of the TRR for the butene and thiazole labels, respectively. Fatty acid-radiolabel association in the remaining matrices was for subcutaneous fat (15 and 52% of the TRR), renal fat (24 and 21% of the TRR) and omental fat (13 and 43% of the TRR) for the thiazole and butene labels, respectively. Association of thiazole and butene labels with proteins was 5 and 34% of the TRR in milk fat and 5 and 15% of the TRR in subcutaneous fat.

Radiolabelled residues were also examined in blood with relation to bovine haemoglobin. It was apparent that radioactivity was associated with the globin-protein in haemoglobin in blood.

Table 1 Total radioactive residues (TRRs) of [^{14}C]fluensulfone in tissues, body fluids and excreta

Matrix	[Thiazole-4-^{14}C]Fluensulfone		[Trifluorobutene-1,2-^{14}C]Fluensulfone	
	mg eq/kg*	% of admin. dose	mg eq/kg*	% of admin. dose
Tissues and Body Fluids				
Liver	2.623	1.67	0.975	0.87
Kidney	1.402	0.20	0.671	0.10
Skim Milk	0.512	1.40	0.297	0.94
Milk Fat	1.977	0.31	0.531	0.12
Flank Muscle	0.217	Not Reported	0.054	Not Reported
Loin Muscle	0.239	4.2[a]	0.040	0.93 [a]
Subcutaneous Fat	0.131	0.01[b]	0.071	0.02 [b]
Omental Fat	0.071	0.04	0.070	0.03
Renal Fat	0.083	0.06	0.043	0.02
Bile	1.412	0.02	0.082	0.00
Blood	0.948	2.76[c]	0.146	0.47 [c]
Excreta				
Faeces	–	15.66	–	12.05
Gastrointestinal Tract	–	2.93	–	2.08
Urine	–	37.49	–	69.66
Cage Wash	–	0.04	–	0.10
Total Recovery	–	66.85	–	87.39

[a] Based on average ^{14}C content, muscle = 50% total goat weight (Luginbuhl, J.M.)

[b] Subcutaneous fat was subsampled and does not accurately represent %AD

[c] Based on blood = 1/12 total goat weight (Haenlein, G.F.W.)

*Values in mg eq/kg taken from extraction data (sum of fractions) except bile (solubilisation) and blood (combustion)

Table 2 Time course of total radioactive residues (TRRs) of [thiazole-4-^{14}C]fluensulfone in milk and excreta

		Skim milk		Milk fat		Urine	Faeces	Total
Sampling Time		mg eq/kg	% of AD	mg eq/kg	% of AD	% of AD	% of AD	% of AD
Day 1	AM	n.d.	–	n.d.	–	0	0	0.08
	PM	0.287	0.07	0.526	0.01			
Day 2	AM	0.29	0.11	0.725	0.06	4.73	2.97	7.99

		Skim milk		Milk fat		Urine	Faeces	Total
Sampling Time		mg eq/kg	% of AD	mg eq/kg	% of AD	% of AD	% of AD	% of AD
	PM	0.455	0.1	1.037	0.02			
Day 3	AM	0.397	0.17	1.179	0.05	7.47	3.73	11.58
	PM	0.546	0.13	1.57	0.03			
Day 4	AM	0.462	0.19	1.728	0.03	8.74	2.44	11.56
	PM	0.631	0.13	2.155	0.03			
Day 5	AM	0.436	0.18	1.863	0.03	8.72	3.03	12.05
	PM	0.323	0.07	1.427	0.02			
Day 6	AM	0.512	0.24	1.977	0.04	7.83	3.49	11.6
Total		1.71% (whole milk)				37.49	15.66	54.86

n.d. = not detected.

Table 3 Time course of total radioactive residues (TRRs) of [trifluorobutene-1,2-^{14}C]fluensulfone in milk and excreta

		Skim milk		Milk fat		Urine	Faeces	Total
Sampling time		mg eq/kg	% of AD	mg eq/kg	% of AD	% of AD	% of AD	% of AD
Day 1	AM	n.d.	–	n.d.	–	0	0	0.12
	PM	0.310	0.11	0.454	0.01			
Day 2	AM	0.122	0.07	0.390	0.01	12.65	2.95	15.80
	PM	0.384	0.11	0.655	0.01			
Day 3	AM	0.152	0.09	0.457	0.01	14.86	2.38	17.48
	PM	0.393	0.12	0.694	0.02			
Day 4	AM	0.145	0.08	0.458	0.01	13.69	1.99	15.91
	PM	0.369	0.12	0.748	0.02			
Day 5	AM	0.119	0.06	0.452	0.01	14.72	2.33	17.15
	PM	0.081	0.02	0.257	0.01			
Day 6	AM	0.297	0.16	0.531	0.02	13.74	2.40	16.32
Total		1.06% (whole milk)				69.66	12.05	82.78

n.d. = not detected.

Table 4 Summary of extraction of radioactive residues from the fluensulfone goat metabolism study

			% TRR					
	TRR (mg eq/kg)		ACN:H_2O or Acetone:Hexane		0.1 M KOH 24% KOH 6 N HCl		PES	
Matrix	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]
Muscle	0.22-0.24	0.04-0.05	36-37	43-53	54-56	26-30	7.8-9.2	16.7-17.5
Kidney	1.40	0.67	40	48	55	50	5.6	1.9
Liver	2.62	0.98	26	28	72	71	2.0	1.1
Skim milk [a]	0.41	0.26	54	64	37	33	9.0	3.5
Milk fat [a]	3.42	0.33	44	64	34	5	n.d.	n.d.
Subcutaneous fat	0.13	0.07	35	80	57	7	0.8	12.7
Renal fat	0.08	0.04	51	61	35	23	14.5	25.6
Omental fat	0.07	0.07	58	74	37	14	5.6	11.4

[a] Milk from Day 6, AM.

n.d. = not detected.

Table 5 Characterization of radioactive residues in kidney

	Kidney			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	1.402	100.0	0.671	100.0
Solvent Extractable (ACN:H_2O)	0.558	39.8	0.322	48.0
Glucose	0.236	16.8	0.090	13.4
Unknowns [a]	0.243	17.4	0.203	30.1
Digestion of PES				
0.1 M KOH	0.029	2.1	0.029	4.3
24% KOH	0.736	52.5	0.137	20.4
6 N HCl (Rinse & Reflux)	–	–	0.170	25.3
Combined Extracts [b] Acidified and Partitioned with EtAc				
Aqueous Phase	0.689	49.1	0.294	43.8
Unknowns [c]	0.689	49.1	0.294	43.8
EtAc Phase	0.076	5.4	0.042	6.3
Unknowns [d]	0.051	3.7	0.023	3.3
PES	0.079	5.6	0.01	1.9

[a] For the thiazole label, there were at least six unknowns which each accounted for 1.1–9.5% of the TRR. For the butene label, there were at least seven unknowns which each accounted for 1.8–9.8% of the TRR.

[b] For the thiazole label, combined extracts are 0.1 M KOH and 24% KOH extracts. For the butene label, combined extracts are 0.1 M KOH, 24% KOH and 6 N HCl.

[c] For the thiazole label, there were at least three unknowns which each accounted for 7.7–26.0% of the TRR. For the butene label, there were at least four unknowns which each accounted for 1.8–30.7% of the TRR. Further work indicates that these were likely to be natural components.

[d] For the thiazole label, there were at least five unknowns which each accounted for 0.2–2.4% of the TRR. For the butene label, there were at least five unknowns which each accounted for 0.3–1.8% of the TRR.

Table 6 Characterization of radioactive residues in liver

	Liver			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	2.623	100.0	0.975	100.0
Solvent Extractable	0.673	25.7	0.276	28.3
Glucose	0.232	8.8	0.039	4.0
Lactose	0.208	7.9	0.036	3.7
Unknowns [a]	0.164	6.2	0.123	12.6
Digestion of PES				
0.1M KOH Extract	0.028	1.1	0.042	4.3
24% KOH Extract	1.328	50.6	0.483	49.5
6 N HCl Extract	0.542	20.7	0.163	16.7
Acidification of Combined Extracts [b] & Partition with EtAc				
Aqueous Phase	1.733	66.1	0.636	65.2
Unknowns [c]	1.711	65.3	0.566	58.2
EtAc Phase	0.165	6.3	0.052	5.3
Unknowns [d]	0.122	4.6	0.032	3.2
PES	0.052	2.0	0.011	1.1

[a] For thiazole labelled liver, there were at least five unknowns which each accounted for 0.6–1.8% of the TRR. For butene labelled liver, there were at least four unknowns which each accounted for 0.8–5.0% of the TRR.

[b] Combined extracts are 0.1 M KOH, 24% KOH and 6 N HCl extracts.

[c] For thiazole labelled liver, there were at least six unknowns which each accounted for 1.1–33.1% of the TRR. For butene

labelled liver, there were at least five unknowns which each accounted for 2.1–36.5% of the TRR. Further work indicates that these were likely to be natural components.

[d] For thiazole labelled liver, there were at least four unknowns which each accounted for 0.3–2.4% of the TRR. For butene labelled liver, there were at least five unknowns which each accounted for 0.4–1.6% of the TRR.

Table 7 Characterization of radioactive residues in skim milk

	Skim Milk			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.409	100.0	0.260	100.0
Solvent extractable	0.221	54.0	0.166	63.8
Lactose	0.187	45.7	0.164	63.1
Unknowns [a]	0.022	5.4	0.002	0.8
Digestion of PES				
Protease	0.151	36.9	0.085	32.7
PES	0.037	9.0	0.009	3.5

[a] For the thiazole label, there were two unknowns which each accounted for 2.2–3.2% of the TRR. For the butene label, there was one unknown.

Table 8 Characterization of radioactive residues in milk fat

	Milk Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	3.416	100.0	0.330	100.0
Solvent extractable	1.489	43.6	0.212	64.2
Clean-up on Silica-Gel				
Hexane Fraction	0.004	0.1	0	0
EtAc:Hexane Fraction	1.446	42.3	0.206	62.4
EtAc Fraction	0.039	1.1	0.006	1.8
Saponification of EtAc:Hexane Fraction & Partition with Hexane:H_2O and Acidified DCM				
Hexane Phase	0.197	5.8	0.122	37.0
Aqueous Phase	0.181	5.3	0.059	17.9
DCM Phase	1.069	31.3	0.025	7.6
Digestion of PES				
Protease	1.165	34.1	0.015	4.5
24% KOH	0.219	6.4	0	0
Loss [a]	0.543	15.9	0.103	31.2
PES [b]	0	0	0	0

[a] Difference in TRR. Loss assumed to be due to conversion to volatile ^{14}C-residues.

[b] No PES remained following digestion with 24% KOH.

Table 9 Characterization of radioactive residues in omental fat

	Omental Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.071	100	0.070	100
Solvent extractable	0.041	57.7	0.052	74.3
Clean-up on Silica-Gel				
Hexane Fraction	0.009	12.7	0.044	62.9
EtAc:Hexane Fraction	0.006	8.5	0.005	7.1

	Omental Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
EtAc Fraction	0.026	36.6	0.004	5.7
Saponification of Hexane Fraction & Partition with (1) Hexane:H_2O and (2) acidified DCM				
Basic Hexane Phase	0	0	0	0
Aqueous Phase	0	0	0.014	20.0
DCM Phase	0.009	12.7	0.030	42.9
Digestion of PES				
0.1 M KOH	0.007	9.9	0.005	7.1
24% KOH	0.019	26.8	0.005	7.1
Combined Alkaline Extracts Acidified and Partitioned with EtAc				
Aqueous Phase	0.021	29.6	–	–
EtAc Phase	0.005	7.0	–	–
PES	0.004	5.6	0.008	11.4

Table 10 Characterization of radioactive residues in subcutaneous fat

	Subcutaneous Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.131	100.0	0.071	100.0
Solvent Extractable (Hexane:Acetone)	0.046	35.1	0.057	80.3
Aqueous Phase	0.010	7.6	0.004	5.6
Clean-up on Silica-Gel of Combined Organic Extracts				
Hexane Fraction	0.020	15.3	0.049	69.0
EtAc:Hexane Fraction	0.008	6.1	0.003	4.2
EtAc Fraction	0.018	13.7	0.005	7.0
Saponification of Hexane Fraction & Partition with (1) Hexane:H_2O and (2) Acidified DCM				
Basic Hexane Phase	0	0	0	0
Aqueous Phase	0	0	0.012	16.9
DCM Phase	0.020	15.3	0.037	52.1
Digestion of PES				
0.1 M KOH	0.019	14.5	0.005	7.0
24% KOH	0.055	42.0	–	–
Combined Alkaline Fractions Partitioned with EtAc				
Aqueous Phase	0.061	46.6	–	–
EtAc Phase	0.013	9.9	–	–
PES	0.001	0.8	0.009	12.7

Table 11 Characterization of radioactive residues in renal fat

	Renal Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR	0.083	100.0	0.043	100.0
Solvent Extractable	0.042	50.6	0.022	51.2
Clean-up on Silica-Gel				
Hexane Fraction	0.020	24.1	0.014	32.6
EtAc:Hexane Fraction	0.006	7.2	0.004	9.3
EtAc Fraction	0.016	19.3	0.004	9.3
Saponification of Hexane Fraction & Partition with (1) Hexane:H_2O and (2) Acidified DCM				
Basic Hexane Phase	0	0	0.002	4.7
Aqueous Phase	0	0	0.003	7.0
DCM Phase	0.020	24.1	0.009	20.9
Digestion of PES				
0.1 M KOH	0.008	9.6	0.004	9.3
24% KOH	0.021	25.3	0.006	14.0
PES	0.012	14.5	0.011	25.6

Table 12 Characterization of radioactive residues in muscle

	Flank Muscle				Loin Muscle			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.217	100.0	0.054	100	0.239	100.0	0.040	100.0
Solvent extractable								
ACN:H_2O Fraction	0.079	36.4	0.023	42.6	0.087	36.4	0.021	52.5
Unknowns [a]	0.073	33.6	0.018	33.4	0.078	32.7	0.023	57.5
Hexane:Acetone	–	–	0.008	14.8	–	–	–	–
Digestion of PES								
0.1 M KOH	0.007	3.2	0.003	5.6	0.009	3.8	0.002	5.0
24% KOH	0.114	52.5	0.011	20.4	0.121	50.6	0.010	25.0
Combined Alkaline Extracts Acidified and Partitioned with EtAc								
Aqueous Phase	0.111	51.2	0.012	22.2	0.119	49.8	0.010	25.0
Unknowns [b]	0.088	40.4	–	–	0.089	37.2	–	–
EtAc Phase	0.010	4.6	0.002	3.7	0.011	4.6	0.002	5.0
PES	0.017	7.8	0.009	16.7	0.02	9.2	0.007	17.5

[a] Flank muscle: thiazole = six unknowns, 3.2–12.4% TRR; butene = five unknowns, 3.7–13.0% TRR. Loin muscle: thiazole = six unknowns, 1.7–20.1% TRR; butene = eight unknowns, 2.5–40.0% TRR. Further work indicates that these were likely to be natural components.

[b] Flank muscle: thiazole = six unknowns, 1.8–23.0% TRR. Loin muscle: thiazole = six unknowns, 2.5–20.1% TRR.

In summary, fluensulfone was not a significant residue in goat tissues or milk. Initially the parent compound is cleaved, displacing butene sulfinic acid which is readily excreted in the urine. However, excretion of the butene half of the molecule is not fully effective and the butene moiety is likely broken down to carbon dioxide and enters the normal metabolic pathways. The thiazole half of the molecule is converted to the thiazole methyl sulfone for excretion, but is not excreted as quickly. Therefore, a much larger portion of the thiazole moiety is incorporated into natural products much in the same way as the butene label. Incorporation of radiolabelled residues into glucose and eventually into lactose takes place mainly in the liver, but is also seen in the kidneys. Lactose is then exported to be excreted in milk. Through the citric acid cycle (i.e. oxaloacetate) radiolabelled residues can also be converted and incorporated into fatty acids and a variety of amino acids (e.g. aspartate) then eventually into triglycerides and proteins.

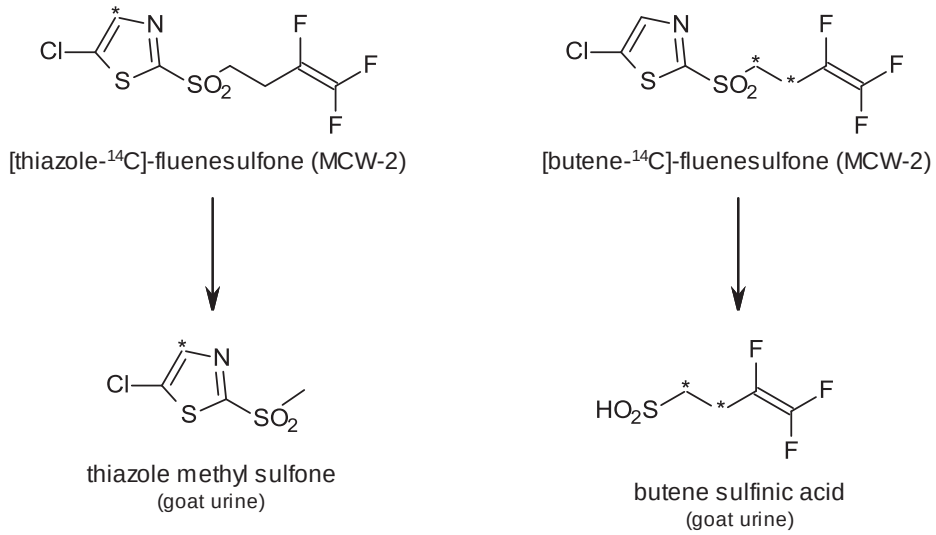


Figure 3 Proposed metabolic pathway of fluensulfone in lactating goat

Laying hens

The metabolism of fluensulfone in laying hens was investigated by LaMar and Quistad (2010, Study R-25454). For each radiolabel position, a group of ten hens was dosed for seven consecutive days at ca. 1.3 mg/bird/day (equivalent to 9.8 ppm in the diet). Eggs were collected twice daily and excreta were collected once daily throughout the study. Hens were sacrificed 20–22 hours after the final dosing, at which point tissues and GI tract (with contents) were collected for analysis.

Tissues, including GI tract with contents, were each homogenized in the presence of dry ice. Total radioactive residues were determined by LSC of solubilized tissues (liver, muscle, and fat) or following combustion (faeces, GI tract). Samples of liver, eggs, and muscle were extracted with twice with ACN:H_2O (1:1, v/v) and once by ACN (neat) for extraction of residues for characterization and identification. Samples of fat were extracted twice with hexane:acetone (4:1, v/v) followed by acetone (neat). Following the extraction procedures, all samples underwent alkaline treatment (KOH in MeOH/H_2O) of the post-extraction solids (PES). Residue analysis for the various extracts was by high-performance liquid chromatography (HPLC) and/or thin-layer chromatography (TLC). Numerous HPLC systems with varying stationary and mobile phases were investigated to achieve satisfactory separation of the radiolabelled components, with detection by UV absorption or refractive index. Identification of metabolites was by co-chromatography with known standards.

In the treated laying hens, 80% (thiazole label) and 79% (butene label) of the AD were recovered. Most of the administered dose was recovered in the excreta and gastrointestinal tracts (76–80%; Table 13). Butene radiolabelled matrices contained consistently higher ^{14}C-residues when compared to the thiazole radiolabel. For example, only 0.15% of the AD for the thiazole radiolabel was excreted in eggs compared to 1.7% for the butene radiolabel. Differences in the amount of total

radioactive residues between the two radiolabels can be attributed to increased incorporation into natural products for the butene label. Thiazole methyl sulfone and butene sulfonic acid were both identified in the excreta. For both radiolabel positions, residues in eggs steadily increased from Day 1 to Day 8 and did not plateau within the dosing period Table 14).

In fat samples, solvent extraction (acetone:hexane) released 81–95% of the TRR. Solvent extraction in liver, egg, and muscle was not as efficient, releasing approximately 13–34% of the total radioactivity from the matrix of interest. Use of basic and/or acidic conditions was required to accomplish more quantitative extraction (Table 15).

The TRRs were highest for liver (thiazole label: 0.64 mg eq/kg; butene label: 1.4 mg eq/kg) and egg (thiazole label: 0.29 mg eq/kg; butene label: 4.06 mg eq/kg). Thiazole-labelled omental and subcutaneous fats (0.04 mg eq/kg and 0.08 mg eq/kg, respectively), contained substantially lower radioactivity compared to butene radiolabelled fat (both 0.31 mg eq/kg). Breast and thigh muscle had the lowest amount of radiolabel in comparison to other tissues; however, butene radiolabelled muscle contained significantly higher residues (0.13 mg eq/kg for both thigh and breast muscles), compared to thiazole radiolabelled muscle (both 0.04 mg eq/kg). No tissues other than liver accounted for more than 0.1% of the AD.

Fluensulfone was detected in omental and subcutaneous fat, (0.009 mg/kg and 0.04 kg/kg for thiazole label, 0.02 mg/kg and 0.04 mg/kg for butene label). Trace amounts of fluensulfone may have been present in other matrices but could not be confirmed due to low levels. With the exception of thiazole sulfonic acid in liver (0.02 mg/kg), no other metabolites of fluensulfone were identified in eggs or tissues. Thiazole methyl sulfone and butene sulfonic acid were identified in faeces. The majority of the radioactivity appeared to be incorporated into natural products such as natural sugars (in liver) fatty acids (in eggs, fat and liver) and in proteins. Comparison of extraction of radioactivity from liver samples treated with and without protease enzyme indicates that ca. 0.16 mg/kg (24% TRR) is associated with proteins and/or amino acids. Incorporation of the radioactivity into triglycerides was noted in both fat matrices and in eggs, and accounted for 7% and 27% of the TRR for the thiazole and butene labels, respectively, in eggs and for 7–12% and 79–87% of the TRR for the thiazole and butene labels, respectively, in the fat matrices. In excreta, the identified residues were the methyl sulfone and BSA metabolites; parent fluensulfone was not observed. The tables below summarize the results of the poultry metabolism study.

Table 13 Total radioactive residues (TRRs) in tissues and excreta

Matrix	Thiazole-labelled Fluensulfone		Butene-labelled Fluensulfone	
	mg eq/kg	% of dose	mg eq/kg	% of dose
Tissues				
Liver	0.643	0.3	1.368	0.7
Eggs	0.286	0.15	4.064	1.71
Omental Fat	0.044	0.0	0.311	0.1
Subcutaneous Fat	0.075	0.0	0.311	0.0
Thigh Muscle	0.043	0.0	0.127	0.1

Matrix	Thiazole-labelled Fluensulfone		Butene-labelled Fluensulfone	
	mg eq/kg	% of dose	mg eq/kg	% of dose
Breast Muscle	0.043	0.0	0.117	0.1
Excreta				
Excreta	–	79.4	–	75.8
Gastrointestinal Tract	–	0.2	–	0.5
Total	–	80.1	–	79.0

Table 14 Total radioactive residues (TRRs) in eggs as function of time

Eggs		(Thiazole-^{14}C)-Label		(Butene-^{14}C)-Label	
		mg eq/kg	% of AD	mg eq/kg	% of AD
Day 1	AM [a]	not detected		not detected	
	PM	–		not detected	
Day 2	AM	0.009	0.00	0.006	0.00
	PM	–		0.050	0.00
Day 3	AM	0.019	0.01	0.218	0.11
	PM	–		0.294	0.01
Day 4	AM	0.029	0.02	0.342	0.17
	PM	–		0.661	0.03
Day 5	AM	0.041	0.02	0.486	0.24
	PM	–		–	
Day 6	AM	0.055	0.03	0.578	0.33
	PM	–		–	
Day 7	AM	0.061	0.03	0.684	0.37
	PM	–		–	
Day 8	AM	0.072	0.04	0.745	0.45
	PM	–		–	
Total		n.a.	0.15	n.a.	1.71

– = No egg production.

n.a. = Not applicable.

[a] Pre-dosing.

Table 15 Extractability of TRRs in tissues

			% TRR					
	TRR (mg eq/kg)		ACN:H_2O or Acetone:hexane		0.1 M KOH 24% KOH 6 N HCl MeOH		PES	
Matrix	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]
Liver	0.60	1.17	13	15	73	84	14	0.4
Egg [a]	0.07	0.68	34	5.2	59	67	0	0
Omental fat	0.04	0.31	81	95	n.d.	n.d.	19	5
Subcutaneous fat	0.08	0.32	83	94	n.d.	n.d.	16	7
Thigh muscle	0.04	0.12	29	17	49	65	22	18
Breast muscle	0.04	0.11	22	20	53	65	25	15

[a] Day 8, morning collection

n.d. = No data

Table 16 Characterization of radioactive residues in liver

	Liver			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (by Sum of Fractions)	0.601	100.0	1.170	100.0
Solvent Extractable	0.078	13.0	0.180	15.4
Thiazole Sulfonic Acid	0.016	2.7	–	–
Unknowns [a]	0.030	5.0	0.164	14.1
Digestion of PES				
0.1 M KOH	0.045	7.5	0.059	5.0
24% KOH	0.334	55.6	0.703	60.1
6 N HCl	0.047	7.8	0.130	11.1
MeOH	0.012	2.0	0.093	7.9
Saponification of Combined Extracts [b] & Partition with (1) Hexane and (2) Acidic DCM				
Basic Hexane Phase	0	0	0	0
Acidic DCM Phase (Analysed by TLC)	0.064	10.6	0.068	5.8
Acidic Aqueous Phase	0.374	62.2	0.917	78.4
Unknowns [c]	0.264	43.9	0.801	68.4
Acidification of Combined Extracts & Partition with Ethyl Acetate				
EtAc Phase	0.203	33.8	0.248	21.2
Loss on Concentration	0.123	20.5	0.175	15.0
EtAc Phase (Analysed by HPLC)	0.080	13.3	0.073	6.2
Unknowns [d]	0.063	10.4	0.044	3.7
Acidic Aqueous Phase	0.235	39.1	0.737	63.0
PES	0.085	14.1	0.005	0.4

[a] For the thiazole label, there were at least four unknowns with two having retention times corresponding to the MCW-2 and methyl sulfone metabolite regions. Each unknown accounted for 0.5–2.7% of the TRR. For the butene label, there were at least five unknowns with one having a retention time corresponding to the MCW-2 region. Each unknown accounted for 0.3–11.5% of the TRR.

[b] Combined extracts are 0.1 M KOH, 24% KOH, 6 N HCl and MeOH Extracts.

[c] For the thiazole label, there were at least six unknowns which each accounted for 3.5–13.1% of the TRR. For the butene label, there were at least 10 unknowns which each accounted for 3.7–22.6% of the TRR.

[d] For the thiazole label, there were seven unknowns which each accounted for 0.7–3.2% of the TRR. For the butene label, there were at least seven unknowns which each accounted for 0.3–0.8% of the TRR.

Table 17 Characterization of radioactive residues in eggs

	Eggs (Day 8, AM)			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (by Sum of Fractions)	0.071	100.0	0.675	100.0
Solvent Extractable with ACN:H_2O	0.024	33.8	0.035	5.2
Hexane Phase (After Partition)	0.005	7.0	0	0
ACN:H_2O Phase	0.019	26.8	0.035	5.2
Unknowns [a]	0.014	19.7	0.034	4.9
Solvent Extractable with Hexane:Acetone	0.005	7.0	0.182	27.0
Hexane Phase	–	–	0	0
DCM Phase	–	–	0.164	24.3
Aqueous Phase	–	–	0.018	2.7
Digestion of PES				
0.1 M KOH Extract	0.005	7.0	0.058	8.6
24% KOH Extract	0.037	52.1	0.400	59.3
Acidification of Combined Extracts [b]& Partition with Ethyl Acetate				
EtAc Phase	0.020	28.2	0.202	29.9

	Eggs (Day 8, AM)			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
Unknowns [c]	0.009	12.6	–	–
Aqueous Phase	0.022	31.0	0.256	37.9
H_2O Rinse (Following C_{18} SPE)	0.011	15.5	0.081	12.0
MeOH Rinse (Following C_{18} SPE)	0.011	15.5	0.175	25.9
Unknowns [d]	–	–	0.172	25.4
PES [e]	0	0	0	0

[a] For the thiazole label, there were at least seven unknowns which each accounted for 1.4–8.5% of the TRR. For the butene label, there were at least six unknowns which accounted for 0.1–1.8% of the TRR.

[b] Combined extracts are the 0.1 M KOH and 24% KOH extracts.

[c] For the thiazole label, there were four unknowns which each accounted for 1.4–5.6% of the TRR.

[d] For the butene label, there were at least 10 unknowns which each accounted for 1.3–6.4% of the TRR.

[e] Following extraction with KOH, no PES remained.

Table 18 Characterization of radioactive residues in omental fat

	Omental Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR	0.043	100.0	0.312	100.0
Solvent Extractable	0.035	81.4	0.297	95.2
Silica-Gel SPE				
Hexane Rinses	0.005	11.6	0.272	87.2
Combined Hexane: EtAc Eluates and ACN Phases	0.030	69.8	0.025	8.0
HPLC Analysis of the Combined Hexane: EtAc:ACN Fractions				
Fluensulfone	0.009	20.9	0.016	5.1
Unknowns [a]	0.020	46.6	0.002	0.6
Saponification of SPE Hexane Fraction and Partitioning with Hexane:H_2O and DCM				
Alkaline Hexane Phase	–	–	0.011	3.5
Acid DCM Phase	–	–	0.237	76.0
Acid Aqueous Phase	–	–	0.024	7.7
PES	0.008	18.6	0.015	4.8

[a] For the thiazole label, there were at least two unknowns which each accounted for 4.7 or 41.9% of the TRR. For the butene label, there were at least two unknowns which each accounted for 0.3% of the TRR.

Table 19 Characterization of radioactive residues in subcutaneous fat

	Subcutaneous Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.075	100.0	0.324	100.0
Solvent Extractable	0.062	82.7	0.303	93.5
Clean-up on Silica-Gel				
Hexane Rinsing	0.006	8.0	0.257	79.3
Hexane: EtAc:ACN Combined	0.056	74.7	0.048	14.8
HPLC				
Fluensulfone	0.041	54.7	0.037	11.4
M1	–	–	0.010	3.1
Unknowns [a]	0.013	17.4	–	–
Saponification of Hexane Fraction and Partitioning				
Alkaline Hexane Phase	–	–	0.013	4.0
Acid DCM Phase	–	–	0.231	71.3

	Subcutaneous Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
Acid Aqueous Phase	–	–	0.014	4.3
Further Extraction of PES with ACN and ACN:H_2O	0.001	1.3	–	–
PES	0.012	16.0	0.021	6.5

[a] For the thiazole label, there were at least three unknowns which each accounted for 2.7–12.0% of the TRR. For the butene label, there were no unknowns.

Table 20 Characterization of radioactive residues in muscle

	Thigh Muscle				Breast Muscle			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.041	100.0	0.121	100	0.036	100.0	0.111	100
Solvent extractable	0.012	29.3	0.020	16.5	0.008	22.2	0.022	19.8
Unknowns [a]	0.008	19.3	0.020	16.5	0.006	16.7	0.015	13.5
Digestion of PES								
0.1 M KOH Extract	0.003	7.3	0.007	5.8	0.002	5.6	0.007	6.3
24% KOH Extract	0.017	41.5	0.072	59.5	0.017	47.2	0.065	58.6
Acidification of Combined Extracts [b] & Partition with EtAc								
EtAc Phase	0.010	24.4	0.015	12.4	0.005	13.9	0.009	8.1
Unknowns [c]	0.010	24.4	–	–	–	–	–	–
Aqueous Phase	0.011	26.8	0.064	52.9	0.014	38.9	0.063	56.8
H_2O Rinse (Following C_{18} SPE)	–	–	0.019	15.7	–	–	0.019	17.1
MeOH Rinse (Following C_{18} SPE)	–	–	0.045	37.2	–	–	0.044	39.6
Unknowns [d]	0.010	24.4	0.041	33.8	0.014	38.8	0.035	31.5
PES	0.009	22.0	0.022	18.2	0.009	25.0	0.017	15.3

[a] For the thiazole labelled thigh muscle, there were at least six unknowns with one having a retention time in the region of MCW-2. Each unknown accounted for 2.4–7.3% of the TRR. For the butene labelled thigh muscle, there were at least three unknowns which accounted each for 5.0–5.8% of the TRR. For the thiazole labelled breast muscle, there were at least six unknowns with one having a retention time in the region of MCW-2. Each unknown accounted for 0–11.1% of the TRR. For the butene labelled breast muscle, there were at least three unknowns which each accounted for 1.8–8.1% of the TRR.

[b] Combined extracts are the 0.1 M KOH and 24% KOH extracts.

[c] For the thiazole labelled thigh muscle, there was only one peak in the fraction.

[d] For the thiazole labelled thigh muscle, there were at least four unknowns which each accounted for 2.4–9.8% of the TRR. For the thiazole labelled breast muscle, there were two unknowns each accounting for 19.4% of the TRR.

In summary, the poultry metabolism study indicates that the parent compound is cleaved displacing butene sulfinic acid, while the thiazole moiety is converted to the thiazole methyl sulfone and thiazole sulfonic acid. Both are eliminated in the excreta. Fluensulfone is broken down to carbon dioxide and subsequently enters normal metabolic pathways. Through the citric acid cycle, radiolabelled residues are converted and incorporated into fatty acids and a variety of amino acids, then eventually into triglycerides and proteins (as seen in fat and liver). The thiazole portion of fluensulfone is excreted at a slightly higher rate. The higher levels of butene radiolabel incorporation

into natural products can be mostly attributed to association with fatty acids, which is not as apparent with thiazole radiolabelled tissues.

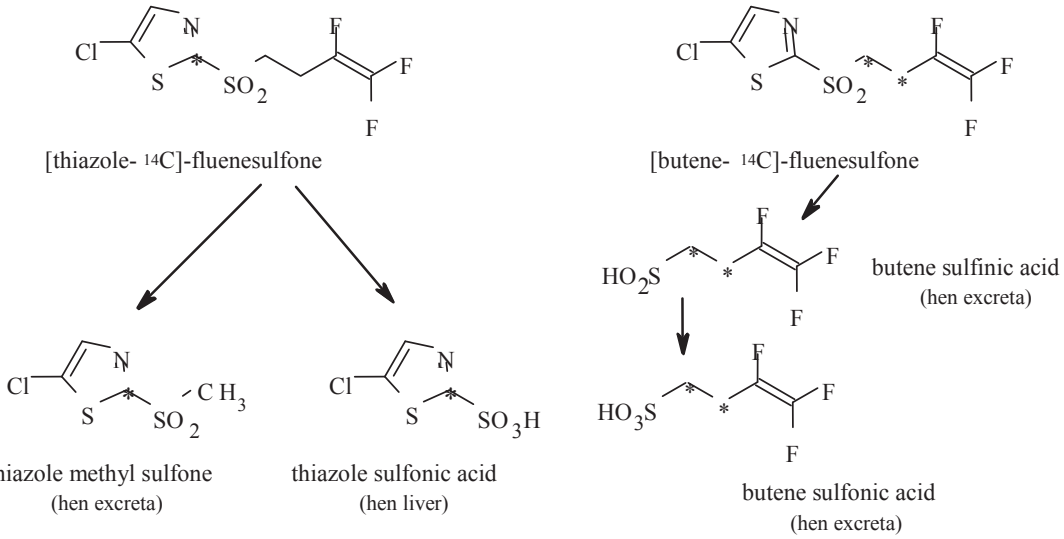


Figure 4 Proposed metabolic pathway of fluensulfone in laying hens

Plant metabolism

The Meeting received studies depicting the metabolism of fluensulfone in tomato, lettuce and potato. All of the studies were conducted with fluensulfone which was radiolabelled, separately, in the thiazole ring and the ethane bridge between the sulfonyl and trifluorobutene moieties.

Fluensulfone was extensively metabolised in all of the studies, with the only major residues being the BSA and TSA metabolites. A few chromatographic fractions had radioactivity in excess of 10% TRR. Investigation of these fractions indicated that the residues were associated with the BSA or TSA metabolites, as salts or other forms of the compounds.

Tomato

The metabolism of fluensulfone was investigated in tomato by Quistad and Bautista (2011, Report OR-25456). For each radiolabel position, an application of fluensulfone, formulated as an emulsifiable concentrate (48% ai), was made to soil at a rate of 4.1 kg ai/ha. Later that same day, tomato seedlings were planted into the treated soil.

Mature tomato fruits were harvested 87 days after treatment. Total radioactive residues were determined by combustion and LSC. Samples were extracted with ACN and ACN:H_2O followed by strong basic hydrolysis for residue characterization and analysis by TLC and/or HPLC. Residue identification was by co-chromatography of the available reference standards. Presence of the known metabolites BSA, MeS, and TSA was confirmed by HPLC-UV, HPLC-MS, and TLC. For unknown

metabolites, the extracts were cleaned up by solid-phase extraction (SPE) with silica-gel columns followed by analytical and semi-preparative HPLC followed by HPLC-MS. No storage stability determination was required as storage time after harvest did not exceed 18 days. Nevertheless a tomato sample containing thiazole labelled residues was reanalysed after 178 days of frozen storage. Fruit was extracted with ACN:H_2O in the same way as the initial fruit sample. HPLC analysis of the combined ACN:H_2O extracts confirmed the stability of the extracts under storage conditions.

Total radioactive residues were higher in samples from the [Bu-^{14}C]fluensulfone treatment than from the [Th-^{14}C]fluensulfone treatment (Table 21). Residues were < 0.001 mg eq/kg in the control sample. There was good agreement between total residues based on the sum of extracted fractions and total residues based on the combustion analysis.

Residues were readily extracted with ACN + ACN:H_2O (Table 22), with the follow-up alkaline extraction releasing only an additional 7–8% of the TRR. No fluensulfone was detected in the tomato samples. The identified residues were predominantly the BSA (42% TRR) and TSA (45% TRR) metabolites from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively (Table 23). From the [Th-^{14}C] treatment, M3, the most abundant unknown metabolite, was considered to be due to the non-retention of TSA, which is a known phenomenon for sulfonic acids. This was confirmed by analysis with and without the presence of matrix which had an effect on peak shape and also by assessing the effects of column loading. Some inter-conversion between M1 and M3 was also noted during these experiments. Further investigation of M1 and M2 suggests that these compounds were salts of TSA. Unresolved radioactivity accounted for 22% of the TRR. From the [Bu-^{14}C] treatment, Fraction F1-F2 in the combined ACN:H_2O extracts accounted for 27% of the TRR and was found to be mainly due to unretained BSA. Fractions F4 and F5 (2–5% of the TRR) were salts of BSA or related compounds. Unresolved radioactivity accounted for 14% of the TRR.

Table 21 Total radioactive residues (TRRs) in tomato following pre-plant application of [^{14}C]fluensulfone

	TRR (mg eq/kg) [a]				
	[Th-^{14}C]		[Bu-^{14}C]		
Matrix	sum of fractions	by combustion	sum of fractions	by combustion	Untreated Control
Tomato Fruits	0.256	0.266	0.517	0.516	< 0.001

[a] Values determined as sum of extracted and unextracted radiocarbon, except for untreated controls which were determined by combustion

Table 22 Extraction summary for tomato fruits after treatment with [^{14}C]fluensulfone

	Radioactive Distribution			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR
ACN:H_2O	0.227	88.67	0.472	91.30
KOH (0.1 M)	0.009	3.52	0.016	3.09
KOH (24%)	0.011	4.30	0.020	3.87
PES	0.009	3.52	0.009	1.74

Total	0.256	100.0	0.517	100.0

Table 23 Radiocarbon detected in tomato fruit following treatment with [^{14}C]fluensulfone

	Tomato Fruit			
	[Th-^{14}C]		[Bu-^{14}C]	
Metabolite/Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.256 (0.266) [a]	100.0	0.517 (0.516)	100.0
Solvent Extractable	0.227	88.7	0.472	91.3
Fluensulfone	–	–	–	–
TSA	0.116	45.4	–	–
M1—Form of TSA	0.009	3.5	–	–
M2—Form of TSA	0.007	2.7	–	–
M3—Form of TSA	0.037	14.5	–	–
M4	0.001	0.4	–	–
M8	< 0.001	0.1	–	–
BSA	–	–	0.215	41.6
F1-F2—Form of BSA	–	–	0.137	26.5
F4—Form of BSA	–	–	0.027	5.2
F5—Form of BSA	–	–	0.011	2.1
Unresolved	0.056	21.9	0.074	14.3

[a] Values in parentheses determined by combustion

Lettuce

The metabolism of fluensulfone was investigated in lettuce by Quistad and Bautista (2011, Report R-25455). For each radiolabel position, an application of fluensulfone, formulated as an emulsifiable concentrate (48% ai), was made to soil at a rate of 4.1 kg ai/ha. Lettuce seeds were planted prior to application.

Samples of lettuce foliage were collected 49 days (immature) and 64 days (mature) after treatment. Within 23 days of harvest, the harvested lettuce samples were homogenized and the TRRs in each sample were determined by combustion analysis and LSC. Samples were extracted with ACN:H_2O and ACN, followed by strong basic hydrolysis. For thiazole-labelled samples, the extract was analysed by HPLC and TLC. For butene-labelled samples, the extract was filtered and the individual residues were then purified by two different HPLC methods. Purified metabolite (butene sulfonic acid) was then analysed via TLC and LC-MS.

Total radioactive residues were higher in samples from the [Th-^{14}C]fluensulfone treatment than from the [Bu-^{14}C]fluensulfone treatment (Table 24). Residues were < 0.001 mg eq/kg in the control sample. There was good agreement between total residues based on the sum of extracted fractions and total residues based on the combustion analysis, although the total by sum of fractions was consistently ca. 87% of that determined by combustion.

Residues were readily extracted with ACN + ACN:H2O (Table 25), with the follow-up alkaline extraction releasing an additional 5–20% of the TRR. Trace levels of fluensulfone were found in the immature lettuce samples from both radiolabel positions. Major residues were the BSA (24%

TRR/38% TRR, immature/mature) and TSA (68% TRR/71% TRR, immature/mature) metabolites from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively (Table 26). From the [Th-14C] treatment, the sum of all other fractions (including unresolved) accounted for 24% of the TRR. Further analysis showed that the separated fractions were salts of TSA and/or other forms of TSA. M3 was found to be polar and due to unretained TSA. M1 was found to be a TSA salt or artifact due to chromatography. Metabolites M4, M5 and M6 were also chromatographic artefacts. Unresolved radioactivity accounted for 6–17% of the TRR. From the [Bu-^{14}C] treatment, the sum of all other fractions (including unresolved) accounted for 46–52% of the TRR. Unresolved radioactivity accounted for 14–24% of the TRR. Further investigation of unidentified fractions showed that most of the fractions were salts or other forms of BSA and/or BSA bound to matrix compounds. Therefore, only BSA is present as a major metabolite with minor amounts of conjugated parent.

Table 24 Total radioactive residues (TRRs) in lettuce following one application of [^{14}C]fluensulfone

	TRR (mg eq/kg) [a]				
	[Th-^{14}C]		[Bu-^{14}C]		
Matrix	sum of fractions	by combustion	sum of fractions	by combustion	Untreated Control
Immature Lettuce (49 DAT)	5.302	6.092	2.071	2.436	< 0.001
Mature Lettuce (69 DAT)	6.145	7.098	1.290	1.548	< 0.001

[a] Values determined as sum of extracted and unextracted radiocarbon, except for untreated controls which were determined by combustion

Table 25Extraction summary for lettuce after treatment with [^{14}C]fluensulfone

	Radioactive Distribution							
	Immature Lettuce (49 DAT)				Mature Lettuce (69 DAT)			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
ACN:H_2O	4.867	91.8	1.582	76.4	5.831	94.9	1.078	83.6
0.1 N KOH	0.201	3.8	0.156	7.5	0.153	2.5	0.095	7.4
24% KOH	0.209	3.9	0.273	13.2	0.145	2.4	0.103	8.0
PES	0.025	0.5	0.060	2.9	0.016	0.3	0.014	1.1
Total	5.302	100.0	2.071	100.0	6.145	100.0	1.290	100.0

Table 26 Metabolites detected in lettuce following treatment with [^{14}C]fluensulfone

		Immature Lettuce				Mature Lettuce			
		[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Metabolite		mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	Sum of Fractions	5.30	100.0	2.071	100.0	6.15	100.0	1.29	100.0
	Combustion	6.09		2.436		7.10		1.55	
Solvent Extractable		4.867	91.8	1.582	76.4	5.831	94.9	1.078	83.6
Fluensulfone		0.009	0.2	0.008	0.4	–	–	–	–
TSA		3.572	67.5	–	–	4.34	70.6	–	–
M1—Form of TSA		0.390	7.4	–	–	0.138	2.2	–	–
M2—Form of TSA		0.372	7.0	–	–	0.191	3.1	–	–
M3—Form of TSA		0.091	1.7	–	–	0.024	0.4	–	–
M4		0.041	0.8	–	–	0.057	0.9	–	–

M5	0.050	0.9	–	–	–	–	–	–
M6	–	–	–	–	0.014	0.2	–	–
BSA	–	–	0.492	23.8	–	–	0.485	37.6
F1-F2—Form of BSA	–	–	0.161	7.7	–	–	0.094	7.3
F4—Form of BSA	–	–	0.104	5.0	–	–	0.019	1.5
F5	–	–	0.183	8.9	–	–	0.072	5.5
F6	–	–	0.227	11.0	–	–	0.054	4.2
F7	–	–	0.032	1.5	–	–	0.007	0.5
F11	–	–	0.035	1.7	–	–	0.008	0.6
F12	–	–	0.005	0.2	–	–	0.032	2.5
Unresolved	0.336	6.3	0.293	14.1	1.067	17.4	0.307	23.8

Potato

The metabolism of fluensulfone was investigated in potato by Quistad and Bautista (2011, Report R-25459). For each radiolabel position, an application of fluensulfone, formulated as an emulsifiable concentrate (48% ai), was made to soil at a rate of 4.0 kg ai/ha ([Th-^{14}C]label) or 4.1 kg ai/ha ([Bu-^{14}C]label). Potato seed pieces were planted prior to application.

Samples of potato tuber were collected 70 days (immature) and 106 days (mature) after treatment. Within 35 days of harvest, the harvested potato tuber samples were homogenized and the TRRs in each sample were determined by combustion analysis and LSC. Samples were extracted with ACN:H_2O and ACN, followed by strong basic hydrolysis ([Bu-^{14}C] treatment only) and strong acid extraction (mature samples only). The initial organic extract was analysed by HPLC and TLC.

Total radioactive residues were higher in samples from the [Th-^{14}C]fluensulfone treatment than from the [Bu-^{14}C]fluensulfone treatment (Table 27). Residues were < 0.001 mg eq/kg in the control sample. There was good agreement between total residues based on the sum of extracted fractions and total residues based on the combustion analysis.

Residues were readily extracted with ACN + ACN:H_2O (Table 28), with the follow-up alkaline extraction releasing an additional 12–22% of the TRR from the [Bu-^{14}C] treated samples. For the mature [Bu-^{14}C] treated sample, the acid extraction released ca. 8% of the TRR. Trace levels of fluensulfone were found in the mature tuber samples from both radiolabel positions (however, this was not confirmed by TLC analysis). Major residues were the BSA (31% TRR/26% TRR, immature/mature) and TSA (63% TRR/65% TRR, immature/mature) metabolites from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively (Table 29). From the [Th-^{14}C] treatment, the sum of all other fractions (including unresolved) accounted for 25–29% of the TRR. The most abundant unidentified fraction in the combined ACN:H_2O extracts was M3 and accounted for 3–7% of the TRR. Further examination showed this was a polar fraction which was considered to be an artifact resulting from the non-retention of TSA. A small amount of M1 was detected (< 2% of the TRR) which may attributable to methyl sulfone, but this was not confirmed by TLC analysis. Unresolved radioactivity accounted for 20–21% of the TRR and was attributed to matrix-bound radioactivity causing smearing within the HPLC column or remaining in the pre-column. Further extraction of the PES (8% of the TRR) was not performed due to the low levels of radioactivity compared the amounts that had been

identified. From the [Bu-^{14}C] treatment, the sum of all other fractions (including unresolved) accounted for 46–50% of the TRR. The most abundant unidentified fraction was the composed fraction F1-F2 in the combined ACN:H_2O extracts which accounted for 16–18% of the TRR. It was found to be mainly due to unretained BSA. Unresolved radioactivity (due to chromatographic artefacts) accounted for 28% of the TRR. Three other fractions F4, F5 and F9, containing < 1% of the TRR, were also resolved but no identification work was carried out due to the very low levels of radioactivity.

Table 27 Total radioactive residues (TRRs) in potato tubers following application of [^{14}C]fluensulfone

	TRR (mg eq/kg) [a]				
	Thiazole Label		Butene Label		
Matrix	sum of fractions	by combustion	sum of fractions	by combustion	Untreated Control
Immature Potato Tubers (70 DAT)	0.335	0.324	0.225	0.222	< 0.001
Mature Potato Tubers (106 DAT)	0.467	0.436	0.163	0.168	< 0.001

[a] Values determined as sum of extracted and unextracted radiocarbon, except for untreated controls which were determined by combustion

Table 28 Extraction summary for potato tubers after treatment with [^{14}C]fluensulfone

	Radioactive Distribution (mg eq/kg)							
	Immature Potato Tubers (70 DAT)				Mature Potato Tubers (106 DAT)			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
ACN:H_2O	0.308	91.94	0.173	76.89	0.428	91.65	0.129	79.14
0.1 N KOH	–	–	0.014	6.22	–	–	0.010	6.13
24% KOH	—	—	0.036	16.00	—	—	0.010	6.13
72% H_2SO_4	—	—	—	—	—	—	0.013	7.98
PES	0.027	8.06	0.002	0.9	0.039	8.35	0.001	0.61
Total	0.335	100.0	0.225	100.0	0.467	100.0	0.163	100.0

Table 29 Radiocarbon detected in potato tubers treated with [^{14}C]fluensulfone

		Immature Potato Tubers (70 DAT)				Mature Potato Tubers (106 DAT)			
		[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Metabolite/Fraction		mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
TRR	Sum of fractions	0.335	100.0	0.225	100.0	0.467	100.0	0.163	100.0
	Combustion	0.324		0.222		0.436		0.168	
Solvent Extractable		0.308	91.9	0.173	76.9	0.428	91.7	0.129	79.1
Fluensulfone		–	–	–	–	0.005	1.1	0.005	3.1
TSA		0.211	63.0	–	–	0.305	65.3	–	–
M1—Form of TSA		0.005	1.5	–	–	0.009	1.9	–	–
M3—Form of TSA		0.023	6.9	–	–	0.016	3.4	–	–
BSA		–	–	0.069	30.7	–	–	0.042	25.8
F1-F2—Form of BSA		–	–	0.037	16.4	–	–	0.029	17.8
F4—Form of BSA		–	–	< 0.001	< 0.1	–	–	0.002	1.2
F5		–	–	0.001	0.4	–	–	0.002	1.2
F9		–	–	0.002	0.9	–	–	0.002	1.2
Unresolved		0.069	20.6	0.064	28.4	0.093	19.9	0.046	28.2

Overall, the metabolism of fluensulfone in tomato, lettuce, and potato is similar and corresponds well with that observed in rotational crop (see below). An overall summary of the metabolic residue profile from the target crops studies is shown in Table 30, followed by the proposed pathway in Figure 5.

Table 30 Summary of results from metabolism studies with fluensulfone in tomato, lettuce, and potato

	Lettuce				Potato					
	Immature		Mature		Immature		Mature		Tomato	
Fraction/ Compound	% TRR	mg equiv./kg	% TRR	mg equiv./kg	% TRR	mg equiv./kg	% TRR	mg equiv./kg	% TRR	mg equiv./kg
[^{14}C-Butene] Fluensulfone										
TRR, mg/kg	2.4		1.6		0.22		0.17		0.52	
Extract	76	1.6	84	1.1	77	0.17	79	0.13	91	0.47
Parent	0.2	0.009	–	–	–	–	3.1	0.005	–	–
BSA [a]	60 (36)	1.2 (0.75)	60 (22)	0.77 (0.29)	47 (18)	0.11 (0.041)	44 (21)	0.071 (0.035)	68 (21)	0.35 (0.06)
TSA [b]	–	–	–	–	–	–	–	–	–	–
Other	14	0.29	24	0.31	30	0.068	32	0.052	22	0.11
Digest	21	0.43	15	0.20	22	0.05	20	0.033	7.0	0.036
PES [c]	2.9	0.06	1.1	0.014	0.9	0.002	0.61	0.001	1.7	0.009
[^{14}C-Thiazole] Fluensulfone										
TRR, mg/kg	6.1		7.1		0.32		0.44		0.27	
Extract	92	4.9	95	5.8	92	0.31	92	0.43	89	0.23
Parent	0.4	0.008	–	–	–	–	1.1	0.005	–	–
BSA [a]	–	–	–	–	–	–	–	–	–	–
TSA [b]	85 (18)	4.5 (1.4)	77 (6.6)	4.8 (0.41)	71 (8.4)	0.24 (0.028)	71 (5.3)	0.33 (0.025)	67 (21)	0.17 (0.06)
Other	6.3	0.34	17	1.1	21	0.069	20	0.096	22	0.056
Digest	7.7	0.41	4.9	0.30	–	–	–	–	7.8	0.02
PES	0.5	0.025	0.3	0.016	8.1	0.027	8.4	0.039	3.5	0.009

[a] Includes fractions shown to be salts and/or chromatographic artefacts of BSA, which are shown parenthetically.

[b] Includes fractions shown to be salts and/or chromatographic artefacts of TSA, which are shown parenthetically.

[c] Post-extraction solids

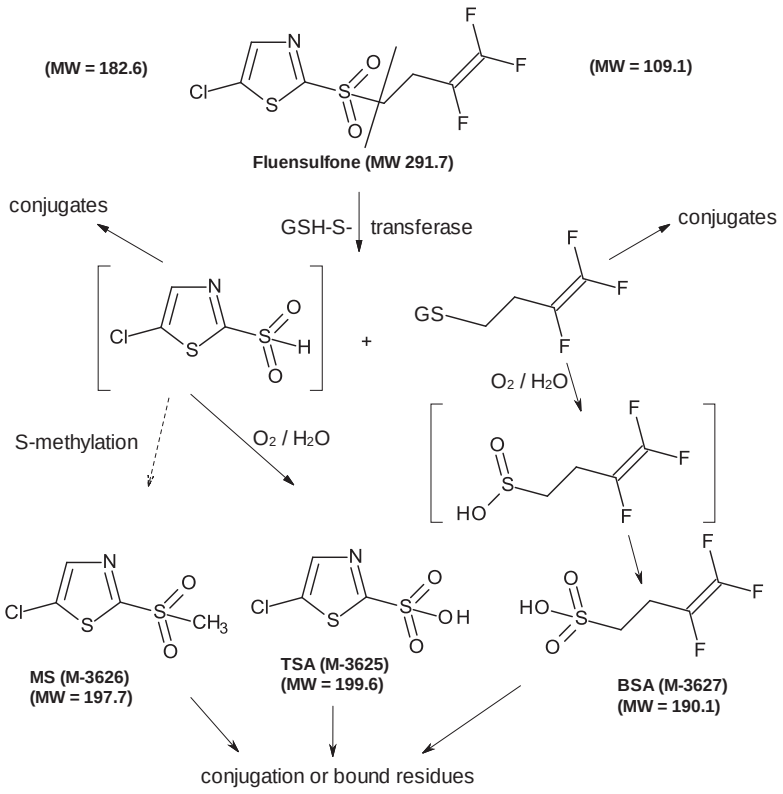


Figure 5 Proposed metabolic pathway of fluensulfone in target and rotational crops

Environmental fate in soil

The Meeting received studies depicting the photodegradation of fluensulfone on soil; aerobic soil metabolism of fluensulfone, TSA, and MeS; and a confined rotational crop study with radish, lettuce, and wheat.

Photolysis

Photolysis of fluensulfone on the surface of soil was investigated by Ponte (2012, Report R-23320) in a study consisting of a preliminary test phase and a definitive test phase. In both phases, [Bu-^{14}C] or [Th-^{14}C] labelled fluensulfone was applied to a medium textured sandy loam soil (Table 31) at a rate of 4 kg/ha. The soil was irradiated with artificial sunlight, continuously, for 14 days, corresponding to 32 days of natural sunlight at 38°N. Soils were maintained at 75% of field moisture capacity (at 1/3 bar) and sampled at various time points throughout the irradiation period. The experimental design included a trapping system to capture volatile organic compounds as well as CO_2. Volatilized radiocarbon was released from foam trap plugs by extraction with ACN. Soils were extracted with acetone:water (4:1, v/v). For each sample matrix, TRRs were determined by LSC of trap solution or extract. For determination of residues, soil extracts were analysed by HPLC-UV and co-chromatographed with known standards; confirmation of metabolites was by TLC.

Table 31 Characteristics of the Soil (Northwood, US) Used

Parameter (units)	Value
Source	Northwood, North Dakota, USA
pH in water	6.8
Cation Exchange Capacity (CEC, meq/100 g)	17
Organic Carbon (%)	2
% Moisture at 1/3 bar	21.9
% Moisture at 15 bar	14
% Moisture at 1/10 bar (pF 2.0)	29.3
Bulk Density (disturbed) (gm/cc)	1.02
Sand (%)	63
Silt (%)	16
Clay (%)	21
USDA Textural Classification	Sandy Loam
FAO Textural Class	Medium
Olsen Phosphorus (ppm)	11
Total Nitrogen (Analyser) (%)	0.16
Soluble Salts (mmhos/cm)	0.17
Base Saturation Data	
Cation	Percent / ppm
Calcium	63.2 / 2152
Magnesium	20.4 / 417
Sodium	0.3 / 13
Potassium	3.8 / 253
Hydrogen	12.2 / 21

In irradiated samples, fluensulfone levels decreased from their initial levels to 52% ([Bu-^{14}C]) or 34% ([Bu-^{14}C]) of the AR (Tables 32-34).

Table 32 Material balance and metabolism of [Th- and Bu-^{14}C]fluensulfone soil photolysis (preliminary test)

	[Th-^{14}C] (% AR)				[Bu-^{14}C] (%AR)			
	Incubation Time In Days							
	0	3	6	6	0	3	6	6
Fraction/Identity		(Light)	(light)	(Dark)		(Light)	(Light)	(Dark)
Fluensulfone	92.1	78.4	59.5	84.6	92.8	70.5	62.3	88.3
Other HPLC peaks	0.0	0.4	0.9	0.0	0.6	0.6	0.1	0.4
Other volatiles in EG [a]	NA	1.5	3.5	0.8	NA	1.3	2.2	0.4
$^{14}CO_2$	NA	6.5	12.3	2.6	NA	1.7	6.9	2.2
Non-extractables	3.2	10.3	16.8	4.9	6.2	21.1	20.1	6.1
Total	95.3	97.1	93.0	92.9	99.6	95.2	91.6	97.4
Mean total ± SD	94.6 ± 2				96 ± 3.4			

[a] Ethylene glycol

Table 33 Material balance and metabolism of [Bu-^{14}C]fluensulfone soil photolysis (definitive test)

	[Bu-^{14}C] (%AR)					
	Incubation Time In Days					
Fraction/Identity	0	2	5	7	9	13
Fluensulfone	91.8	82.9	71.5	74.6	56.2	52.2
Others [a]	0.3	0.2	1.8	1.0	3.9	4.9
Non-extractables	3.7	12.2	20.2	16.0	16.5	19.4

EG Trap	NS	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
NaOH Trap	NS	1.1	< 1.8	3.1	8.2	8.4
ACN Trap	NS	0.6	< 0.9	0.7	2.5	2.6
Total	95.8	96.9	95.9	95.2	87.5	87.4
Mean total ± SD	93.1 ± 4.4					

NS = Not Sampled

[a] Corresponds to at least six fractions.

Table 34 Material balance and metabolism of [Th-^{14}C]fluensulfone soil photolysis (definitive test)

	[Th-^{14}C] (%AR)		
	Incubation Time in Days		
Fraction/Identity	0	4	14
Fluensulfone	83.5	78.4	34.4
TSA	0.2	0.3	8.6
Others	0.7	0.8	1.1
Non-extractables	6.2	10.0	16.4
Foam plug trap	1.0	0.4	3.8
2 N H_2SO_4 trap	0.5	0.1	2.7
NaOH trap	4.3	1.3	19.9
Total	96.3	91.3	86.9
Mean total ± SD	91.5 ± 4.7		

Aerobic soil metabolism (Fluensulfone)

The metabolism and degradation kinetics of fluensulfone in aerobic soils was investigated by Moser (2011, Report R-27436). In that study, [Bu-^{14}C] or [Th-^{14}C] labelled fluensulfone was applied at a rate of 4 kg/ha to six different soils (Table 35). The soils were incubated under dark, aerobic conditions at 20 °C for 120 days. Samples were collected at various time points throughout the study, extracted first with $CaCl_2$ and then with ACN:H_2O and analysed for residues by LSC, HPLC, and/or TLC. In addition, the Fislis soil underwent Soxhlet extraction and analysis by LSC and TLC.

Table 35 Characteristics of the soils used in the aerobic metabolism study for fluensulfone

Parameter	Value					
Name	Fislis	Hagenthal	Horn	Montesquieu	Senozan	Sevelen
pH ($CaCl_2$)	6.75	7.13	7.23	7.36	7.54	7.36
Organic carbon %	2.13	1.65	2.36	1.5	0.61	1.61
CEC (meq/100 g soil)	22.99	18.79	21.72	21.09	13.63	9.09
Soil type	silt loam	silt loam	loam	clay loam	loam	sandy loam
Bulk density [kg/dm^3]	1.08	1.22	0.99	1.18	1.21	1.18
Particle size analyses (mm):						
0.002 (clay) [%]	26.42	24.42	25.11	38.70	20.58	9.51
0.002–0.05 (silt) [%]	65.57	53.51	36.22	31.84	35.25	36.96
0.05–2.0 (sand) [%]	8.01	22.07	38.67	29.46	44.17	53.53
Water holding capacity (g water/100 g soil):						
at pF 1.0	75.62	56.80	73.15	59.76	48.77	58.94
at pF 2.0	39.65	36.88	33.52	33.52	29.97	31.48
at pF 2.5	30.98	25.83	28.47	25.91	19.52	21.45
Biomass determination as mg C/100 g soil (%)						
pre-study	26.9 (1.3)	22.5 (1.4)	15.1 (0.6)	26.9 (1.8)	26.9 (4.4)	18.1 (1.1)
test initiation	28.0 (1.3)	22.5 (1.4)	39.1 (1.7)	22.5 (1.5)	17.0 (2.8)	22.5 (1.4)
mid-study	22.5 (1.1)	22.5 (1.4)	22.5 (1.0)	28.1 (1.9)	17.0 (2.8)	17.0 (1.1)
test end	18.1 (0.8)	28.0 (1.7)	33.6 (1.4)	17.0 (1.1)	17.0 (2.8)	22.5 (1.4)

Table 36 Distribution of applied radioactivity following application of [^{14}C]fluensulfone to six soils

		Percent of applied radioactivity, [Bu-^{14}C]/ [Th-^{14}C]						
Soil	Day	$CaCl_2$ extract	Organic extract	Total extractable	Soil bound	$^{14}CO_2$	VOC	Total recovered
Fislis	0	18.8/24.1	68.8/68.5	87.6/92.6	9.8/4.6	NA/NA	NA/NA	97.4/97.2
	2	18.8/22.8	59.7/66.4	78.5/89.2	15.5/8.0	4.6/0.7	< 0.1/< 0.1	98.6/97.9
	7	15.6/27.2	51.5/59.9	67.1/87.1	19.0/12.3	0.6 [a]/1.9	< 0.1/< 0.1	86.7 [a]/101.4
	14	13.2/29.4	33.8/53.9	47.1/83.3	31.5/10.3	39.1/4.3	0.1/< 0.1	117.8 [b]/97.9
	21	11.3/30.5	31.8/50.9	43.1/81.4	29.9/11.3	1.1/5.3	< 0.1/< 0.1	74.1 [a]/98.1
	28	9.6/27.3	27.5/53.0	37.1/80.3	33.4/9.8	29.6/5.1	< 0.1/< 0.1	100.1/95.2
	50	6.8/33.0	12.8/45.3	19.7/78.2	37.8/12.7	44.3/7.4	< 0.1/< 0.1	101.8/98.3
	77	2.6/NS	3.2/NS	5.8/NS	43.9/NS	55.7/NS	< 0.1/NS	105.5/NS
	90	1.9/NS	3.0/NS	4.8/NS	38.8/NS	55.5/NS	< 0.1/NS	99.1/NS
	120	0.5/33.1	1.7/39.6	2.2/72.7	40.1/6.0	11.2/16.8	< 0.1/< 0.1	53.6 [a]/95.5
Hagenthal	0	28.4/30.2	61.8/64.6	90.2/94.9	6.5/3.9	NA/NA	NA/NA	96.7/98.7
	2	22.6/28.6	57.9/60.7	80.5/89.3	12.7/5.9	5.5/0.5	< 0.1/< 0.1	98.7/95.7
	7	18.4/32.8	43.2/55.3	61.5/88.1	23.7/10.4	12.5/1.7	< 0.1/< 0.1	97.8/100.2
	14	12.6/35.9	24.7/47.4	37.3/83.4	31.7/11.3	23.0/3.7	< 0.1/< 0.1	92.0/98.4
	21	15.2/35.4	25.9/45.2	41.0/80.6	26.7/10.5	28.2/5.8	0.1/< 0.1	96.0/96.9
	28	11.5/32.5	21.0/48.2	32.5/80.6	28.4/11.7	39.8/6.3	< 0.1/< 0.1	100.7/98.6
	50	9.2/38.9	10.8/36.3	20.0/75.2	30.1/12.0	36.5/7.1	< 0.1/< 0.1	86.6 [a]/94.3
	77	1.0/NS	1.7/NS	2.7/NS	38.5/NS	36.8/NS	< 0.1/NS	78.0 [a]/NS
	90	0.6/NS	1.2/NS	1.9/NS	37.7/NS	29.7/NS	< 0.1/NS	69.2 [a]/NS
	120	0.6/32.1	1.4/29.2	2.0/61.3	34.7/12.3	52.2/20.3	< 0.1/< 0.1	88.9 [a]/93.9
Horn	0	20.8/23.4	65.8/68.7	86.6/92.1	8.8/5.8	NA/NA	NA/NA	95.5/97.9
	2	17.1/22.7	57.5/66.0	74.6/88.7	18.0/10.9	5.1/0.1	< 0.1/< 0.1	97.7/99.6
	7	14.7/25.7	40.5/58.8	55.2/84.5	27.8/13.4	16.0/0.2	< 0.1/< 0.1	99.0/98.2
	14	10.8/29.9	40.5/50.7	51.4/80.6	28.1/14.4	15.0/0.3	< 0.1/< 0.1	94.6/95.3
	21	10.5/35.9	22.0/47.4	32.5/83.3	30.9/12.9	31.8/10.5	< 0.1/< 0.1	95.2/106.8
	28	7.3/27.4	21.0/51.0	28.3/78.4	34.9/13.3	36.9/8.4	< 0.1/< 0.1	100.2/100.2
	50	3.5/33.4	4.3/43.2	7.8/76.6	41.9/12.4	50.7/9.8	< 0.1/< 0.1	100.4/98.9
	77	0.4/NS	1.6/NS	2.0/NS	37.9/NS	40.9/NS	< 0.1/NS	80.8 [a]/NS
	90	1.3/NS	2.2/NS	3.5/NS	42.2/NS	51.7/NS	0.3/NS	97.6/NS
	120	0.4/27.7	1.6/38.3	2.0/66.0	32.7/14.4	54.6/20.6	< 0.1/< 0.1	89.3 [a]/101.0
Montesquieu	0	28.1/25.5	63.6/66.4	91.7/91.9	6.9/3.8	NA/NA	NA/NA	98.6/95.7
	2	23.5/27.5	59.0/63.4	82.5/90.8	11.8/6.9	2.3/0.4	< 0.1/< 0.1	96.6/98.1
	7	17.9/29.8	47.0/56.9	64.9/86.8	22.5/9.6	8.2/1.2	< 0.1/< 0.1	95.7/97.7
	14	18.2/32.8	36.4/51.4	54.6/84.1	28.3/11.6	15.7/3.4	< 0.1/< 0.1	98.6/99.2
	21	16.3/34.7	33.0/48.6	49.3/83.3	28.9/9.3	23.0/5.0	< 0.1/< 0.1	101.2/97.6
	28	12.4/30.9	28.4/49.5	40.9/80.4	29.4/13.1	27.4/5.1	< 0.1/< 0.1	97.6/98.7
	50	8.8/35.6	13.5/40.3	22.3/75.9	38.6/14.0	36.8/6.5	0.1/< 0.1	97.9/96.5
	77	3.2/NS	3.7/NS	7.0/NS	49.4/NS	45.8/NS	< 0.1/NS	102.1/NS
	90	1.2/NS	2.1/NS	3.2/NS	43.5/NS	46.0/NS	< 0.1/NS	92.7/NS
	120	0.4/35.4	1.5/34.9	1.9/70.3	36.1/11.9	43.8/13.4	0.5/< 0.1	82.3 [a]/95.6
Senozan	0	40.2/40.3	57.4/57.3	97.6/97.6	4.5/2.7	NA/NA	NA/NA	102.0/100.3
	2	33.8/36.2	55.5/57.4	89.3/93.6	8.0/4.4	2.1/0.6	< 0.1/0.2	99.4/98.8
	7	25.9/36.0	45.4/53.3	71.3/89.3	18.9/6.9	8.1/1.6	< 0.1/< 0.1	98.3/97.9
	14	22.9/37.5	35.5/51.8	58.4/89.3	21.5/6.7	31.8/2.6	0.1/< 0.1	111.9 [b]/98.7
	21	17.4/39.7	27.4/48.7	44.8/88.4	32.7/9.1	15.7/0.8	< 0.1/< 0.1	93.2/98.4
	28	15.9/30.3	33.7/54.1	49.6/84.4	25.3/8.7	11.5 [a]/5.5	< 0.1/< 0.1	86.4/98.7
	50	18.6/37.7	27.6/45.6	46.2/83.3	28.8/8.5	23.6/6.0	< 0.1/< 0.1	98.7/97.8
	77	15.0/NS	19.8/NS	34.9/NS	29.3/NS	26.9/NS	< 0.1/NS	91.1/NS
	90	16.7/NS	21.9/NS	38.6/NS	25.0/NS	28.9/NS	< 0.1/NS	92.5/NS
	120	12.7/36.0	13.2/37.8	25.9/73.8	25.9/11.4	28.1 [a]/11.7	0.4/0.1	80.3 [a]/97.0
Sevelen	0	29.1/30.3	63.3/64.3	92.4/94.6	8.0/5.0	NA/NA	NA/NA	100.4/99.6
	2	25.6/29.1	54.1/60.1	79.7/89.3	12.5/7.6	3.7/0.1	< 0.1/< 0.1	95.9/97.0
	7	20.7/30.1	45.0/55.3	65.7/85.4	20.7/10.5	16.1/4.4	< 0.1/< 0.1	102.4/100.3
	14	18.1/32.7	33.6/48.8	51.7/81.5	25.8/12.5	17.6/5.3	< 0.1/< 0.1	95.1/99.3
	21	16.5/33.3	28.0/44.7	44.5/77.9	24.3/12.0	25.0/4.1	< 0.1/< 0.1	93.8/94.0

		Percent of applied radioactivity, [Bu-^{14}C]/ [Th-^{14}C]						
Soil	Day	$CaCl_2$ extract	Organic extract	Total extractable	Soil bound	$^{14}CO_2$	VOC	Total recovered
	28	12.7/32.8	22.0/41.8	34.6/74.6	29.7/15.2	30.6/7.3	< 0.1/< 0.1	94.9/97.2
	50	8.2/31.8	9.2/34.9	17.4/66.7	33.1/12.9	35.1/16.5	< 0.1/< 0.1	85.6 [a]/96.0
	77	3.4/NS	3.0/NS	6.4/NS	33.7/NS	50.4/NS	< 0.1/NS	90.5/NS
	90	1.8/NS	2.3/NS	4.1/NS	36.9/NS	53.3/NS	< 0.1/NS	94.3/NS
	120	1.0/25.4	1.4/23.2	2.5/48.5	32.6/14.6	52.0/30.3	< 0.1/< 0.1	87.1 [a]/93.5

[a] Due to losses of $^{14}CO_2$

[b] The KOH trap was probably mistakenly exchanged for another sample (cf. day 21).

NS = No Sample

Table 37 Formation of major soil metabolites of fluensulfone in six aerobic soils

		Percent of applied radioactivity			
Soil	Day	Fluensulfone ([Bu-^{14}C]/ [Th-^{14}C])	BSA	TSA	MeS
Filsis	0	86.4/83.2	1.2	9.4	0.0
	2	77.1/74.5	1.4	14.7	0.0
	7	48.6/45.6	18.5	41.5	0.0
	14	35.4/27.1	11.6	53.8	2.4
	21	30.4/23.8	12.7	53.1	4.6
	28	23.2/17.6	13.9	59.3	3.4
	50	7.9/5.6	11.8	68.5	4.2
	77	2.1/NS	3.7	NS	NS
	90	1.9/NS	2.9	NS	NS
	120	1.0/0.0	1.2	72.7	0.0
Hagenthal	0	90.2/87.6	0.0	7.3	0.0
	2	76.2/73.1	4.4	16.2	0.0
	7	47.0/47.3	14.6	40.8	0.0
	14	26.0/20.0	11.1	61.0	2.4
	21	22.3/11.7	18.7	64.4	4.5
	28	15.9/10.5	16.7	64.6	5.5
	50	5.5/2.3	14.5	69.7	3.2
	77	0.9/NS	1.8	NS	NS
	90	0.6/NS	1.2	NS	NS
	120	0.7/0.0	1.3	61.3	0.0
Horn	0	81.9/81.8	4.7	10.3	0.0
	2	70.0/70.6	4.6	18.0	0.0
	7	47.1/37.9	8.1	46.6	0.0
	14	37.1/16.3	14.3	58.8	5.5
	21	16.3/9.8	16.2	68.7	4.9
	28	8.9/5.8	19.4	68.8	3.8
	50	1.3/0.0	5.7	76.6	0.0
	77	0.5/NS	1.2	NS	NS
	90	0.7/NS	2.4	NS	NS
	120	0.5/0.0	1.2	66.0	0.0
Montesquieu	0	90.0/86.8	1.7	5.2	0.0
	2	79.6/86.0	2.9	4.8	0.0
	7	50.1/56.7	14.9	30.0	0.0
	14	40.1/30.9	14.5	53.2	0.0
	21	32.0/33.4	17.3	49.9	0.0
	28	12.7/19.0	28.1	57.2	4.2
	50	8.3/5.5	14.1	65.0	5.4
	77	2.4/NS	4.6	NS	NS
	90	1.2/NS	2.0	NS	NS
	120	0.9/0.0	1.0	70.3	0.0
Senozan	0	97.6/93.4	0.0	4.2	0.0
	2	89.3/90.0	0.0	3.6	0.0

		Percent of applied radioactivity			
Soil	Day	Fluensulfone ([Bu-^{14}C]/ [Th-^{14}C])	BSA	TSA	MeS
	7	62.6/59.8	8.7	29.6	0.0
	14	48.8/55.0	9.7	34.3	0.0
	21	31.0/36.1	13.8	48.4	3.9
	28	32.9/32.4	16.7	48.4	3.6
	50	21.1/19.8	25.1	59.7	3.8
	77	8.7/NS	26.2	NS	NS
	90	7.6/NS	31.0	NS	NS
	120	2.2/0.0	23.8	73.8	0.0
Sevelen	0	92.4/89.8	0.0	4.8	0.0
	2	75.0/82.4	4.7	6.9	0.0
	7	48.3/37.1	17.4	48.3	0.0
	14	34.4/21.2	17.3	57.8	2.5
	21	NS/NS	NS	NS	NS
	28	15.1/8.7	19.5	58.5	7.5
	50	2.5/2.1	14.9	58.4	6.2
	77	0.8/NS	5.6	NS	NS
	90	0.6/NS	3.5	NS	NS
	120	0.4/0.0	2.1	48.5	0.0

NS = No Sample

Table 38 Summary of half-life estimates for fluensulfone and BSA in six soils

Soil	Fislis	Hagenthal	Horn	Montesquieu	Senozan	Sevelen
Type	Silt loam	Silt loam	Loam	Clay loam	Loam	Sandy loam
Model	SFO [a]	SFO	SFO	SFO	SFO	SFO
Residue	Half-life (days)					
Fluensulfone	10.5	7.6	7.2	11.1	16.5	7.1
BSA	19.7	22.6	21.9	17.8	[b]	26.3

[a] SFO = Single First-Order

[b] Degradation rate of BSA could not be calculated due to insufficient data points

Aerobic soil degradation rate (TSA)

The degradation rate of TSA metabolite of fluensulfone in three aerobic soils was investigated by Brands (2011, R-28470). In that study, Fislis, Horn, and Sevelen soils (see fluensulfone aerobic soil metabolism section above) were treated with the test substance at a nominal concentration of 3.2 mg/kg dry soil and incubated, in the dark, for 150 days. Duplicate samples were collected at nine time points throughout the study, extracted with ACN:H_2O (50:50, v/v), and analysed by HPLC-MS/MS.

Overall procedural recoveries from freshly fortified soils ranged from 95–112% of the applied amount (Table 39) and levels of TSA showed a slow decline over the incubation period (Table 40). Single first-order half-life estimates for TSA were 560 days for Fislis soil, 450 days for Horn soil, and 230 days for Sevelen soil.

Table 39 Procedural recovery of TSA from soils fortified at 3.2 mg/kg

	Fislis		Horn		Sevelen	
Sample time ID	TSA (mg/kg)	Recovery (% of nominal)	TSA (mg/kg)	Recovery (% of nominal)	TSA (mg/kg)	Recovery (% of nominal)
7	3.25	101	3.39	105	3.48	108
15	3.4	106	3.29	102	3.43	107
28	3.4	106	3.33	104	3.48	108
42	3.59	112	3.55	110	3.13	97
60	3.18	100	3.03	95	3.13	98
91	3.14	98	3.26	102	3.14	98
120	3.32	104	3.12	98	3.45	108
150	3.45	107	3.36	105	3.17	99

Table 40 Levels of TSA in three soils incubated for 150 days, normalized to Time 0

Time (days)	Fislis	Horn	Sevelen
0	100, 100	100, 100	100, 100
7	109, 106	98, 101	88, 105
15	101, 96	95, 108	87, 97
28	93, 94	92, 100	83, 96
42	90, 96	90, 94	86, 89
60	85, 82	76, 83	74, 77
91	93, 94	82, 90	64, 81
120	88, 86	88, 90	67, 74
150	83, 88	163 [a], 0 [a]	57, 70

[a] Unexpected results were not used for calculation of DT_{50} and DT_{90}

Aerobic soil degradation rate (MeS)

The degradation rate of MeS metabolite of fluensulfone in three aerobic soils was investigated by Brands (2011, R-28472). In that study, Fislis, Horn, and Sevelen soils (see fluensulfone aerobic soil metabolism section above) were treated with the test substance at a nominal concentration of 0.4 or 0.04 mg/kg dry soil and incubated, in the dark, for 120 days. Duplicate samples were collected at eight time points throughout the study, extracted with ACN:H_2O (50:50, v/v), and analysed by HPLC-MS/MS.

Overall procedural recoveries from freshly fortified soils ranged from 95–112% of the applied amount (Table 41) and levels of MeS showed a slow decline over the incubation period (Table 42). Single first-order half-life estimates for MeS were 41 days for Fislis soil, 28 days for Horn soil, and 30 days for Sevelen soil.

Table 41 Procedural recovery of MeS from soils fortified at 0.4 or 0.04 mg/kg

	Fislis		Horn		Sevelen	
Sample time ID	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)
7	0.393	98	0.338	85	0.357	89
15	0.406	102	0.361	90	0.366	92
28	0.469	117	0.408	102	0.349	87
42	0.0418	104	0.0435	108	0.0369	92
60	0.0395	98	0.0403	100	0.0418	104

	Fislis		Horn		Sevelen	
Sample time ID	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)
91	0.0391	97	0.0395	99	0.0378	94
120	0.0441	110	0.0393	100	0.0415	103

Table 42 Levels of MeS in three soils incubated for 150 days, normalized to Time 0

Time (days)	Fislis	Horn	Sevelen
0	100, 100	100, 100	100, 100
7	95, 111	85, 78	78, 83
15	84, 89	57, 67	62, 60
28	61, 67	47, 42	37, 44
42	48, 54	36, 34	39, 35
60	38, 41	23, 24	26, 30
91	22, 23	14, 14	17, 17
120	14, 16	8, 7	10, 10

Anaerobic soil metabolism

No anaerobic soil metabolism studies were provided.

Confined rotational crop studies

The fate of fluensulfone as relates to rotational crops was investigated by Quistad *et al*. (2011, Report OR-25457). In that study, radish, lettuce and wheat were planted into test boxes that had been treated with [Bu-^{14}C] or [Th-^{14}C] labelled fluensulfone at a rate of ca. 4 kg/ha. The crops were planted into the test boxes at 30, 120, and 360 days after treatment (390 days for lettuce due to crop failure at the 360-day plant-back interval). At each plant-back interval (PBI), samples consisted of radish roots and radish tops; lettuce leaves; and wheat forage, grain, hay, and straw.

After harvest, the samples were homogenized and an aliquot was taken for TRR determination by combustion and LSC. In addition, samples were extracted initially with ACN:H_2O (1:1, v/v) and ACN, followed by strong basic and, in some cases, acidic hydrolysis. Extracted residues were analysed by TLC and/or HPLC (UV and radio-chromatography via fraction collection and LSC) for residue determination. Multiple TLC systems and HPLC conditions were used to obtain adequate separation and analysis.

Total radioactive residues in the rotational crops are shown in Table 43. There was generally good agreement between TRR by combustion and TRR by sum of fractions. The TRR levels from the [Th-^{14}C] treatments were higher from than those from the [Bu-^{14}C] treatments and tended to show a plateau between the 120-day and 360/390-day PBIs that was not seen with the [Bu-^{14}C] treatments.

The ACN:H_2O solution was able to extract the majority of the TRR from all of the rotational crop matrices (Tables 44–47). Analysis of the extracts showed levels of fluensulfone in radish (Tables 48–51), lettuce (Tables 52–55), and wheat (Table 56–63) samples from at least one PBI/radiolabel position/sample matrix combination. In all cases, the occurrence of fluensulfone was ≤ 5.1% TRR and

was higher in samples from the [Bu-^{14}C] treatments. The major residues in all matrices were TSA and BSA from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively. Across PBIs, levels of BSA generally declined in terms of both absolute concentration and in terms of %TRR. Absolute levels of TSA generally declined with increasing PBI, especially between the 30-day and 120-day PBIs, but increased in terms of %TRR over the course of the study. Numerous minor metabolites and/or fractions were observed. Most of these were attributed to salts or chromatographic artifacts of TSA or BSA.

Table 43 Summary of TRRs in rotational crops at each plant-back interval

	TRRs [a] (mg eq/kg)					
Crop	[Th-^{14}C]			[Bu-^{14}C]		
PBI	30 DAT	120 DAT	360 DAT	30 DAT	120 DAT	360 DAT
Radish (foliage)	5.26 (5.76)	1.76 (1.90)	2.86 (3.58)	0.48 (0.54)	0.47 (0.51)	0.04 (0.04)
Radish (roots)	0.79 (0.83)	0.44 (0.45)	0.38 (0.39)	0.15 (0.19)	0.10 (0.08)	0.01 (0.01)
Lettuce (immature)	0.65 (0.58)	0.71 (0.81)	0.13 (0.13) [b]	0.31 (0.33)	0.05 (0.04)	0.05 (0.05) [b]
Lettuce (mature)	0.57 (0.60)	0.33 (0.34)	0.34 (0.33)	0.20 (0.21)	0.05 (0.04)	0.02 (0.01)
Wheat (forage)	16.6 (19.2)	2.96 (3.42)	3.33 (3.19)	2.53 (3.17)	0.71 (0.84)	0.06 (0.07)
Wheat (straw)	18.6 (18.5)	3.52 (3.85)	6.64 (7.26)	1.94 (1.99)	0.30 (0.31)	0.17 (0.16)
Wheat (grain)	0.36 (0.36)	0.30 (0.32)	0.34 (0.35)	0.17 (0.17)	0.06 (0.07)	0.04 (0.04)
Wheat (hay)	27.0 (26.4)	9.40 (9.29)	10.8 (11.3)	4.50 (4.35)	0.37 (0.36)	0.13 (0.14)

[a] Values in parenthesis obtained by direct combustion

[b] 390 day lettuce samples since 360-day lettuce was replanted because of crop failure

DAT = Days after treatment.

Table 44 Extraction summary for radish foliage and roots after soil treatment with [^{14}C]fluensulfone

Crop	Radish							
Matrix	Foliage				Roots			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	5.166	98.2	0.452	94.4	0.723	91.2	0.126	86.3
0.1 N KOH Extract	0.053	1.0	0.010	2.1	0.011	1.4	0.008	5.5
24% KOH Extract	0.033	0.6	0.013	2.7	0.023	2.9	0.008	5.5
PES	0.011	0.2	0.004	0.8	0.036	4.5	0.004	2.7
Total	5.263		0.479		0.793		0.146	
PBI	120 DAYS							
ACN:H_2O Extract	1.709	97.3	0.436	93.4	0.382	87.4	0.079	76.0
0.1 N KOH Extract	0.021	1.2	0.006	1.3	0.009	2.1	0.006	5.8
24% KOH Extract	0.020	1.1	0.023	4.9	0.026	5.9	0.015	14.4
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	–	–	–	–	0.002	1.9
Aqueous Phase	–	–	–	–	–	–	0.019	18.3
PES	0.006	0.3	0.002	0.4	0.020	4.6	0.004	3.8
Total	1.756		0.467		0.437		0.104	
PBI	360 DAYS							
ACN:H_2O Extract	2.842	99.4	0.031	81.6	0.365	96.3	0.006	50.0
0.1 N KOH Extract	0.007	0.2	0.001	2.6	0.001	0.3	< 0.001	0.0
24% KOH Extract	0.010	0.4	0.005	13.2	0.009	2.4	0.005	41.7
PES	0.001	0.0	0.001	2.6	0.004	1.1	0.001	8.3
Total	2.860		0.038		0.379		0.012	

Table 45 Extraction summary for immature and mature lettuce after soil treatment with [^{14}C]fluensulfone

Crop	Lettuce							
Matrix	Immature				Mature			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	0.495	76.5	0.221	71.1	0.494	87.4	0.137	67.2
Acidification with HCl & Partition with EtAc								
EtAc Phase	0.196	30.3	–	–	–	–	–	–
Aqueous Phase	0.299	46.2	–	–	–	–	–	–
0.1 N KOH Extract	0.038	5.9	0.030	9.6	0.023	4.1	0.017	8.3
24% KOH Extract	0.099	15.3	0.055	17.7	0.043	7.6	0.041	20.1
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	0.018	5.8	0.016	2.8	0.010	4.9
Aqueous Phase	–	–	0.067	21.5	0.050	8.8	0.048	23.5
PES	0.015	2.3	0.005	1.6	0.005	0.9	0.009	4.4
Total	0.647		0.311		0.565		0.204	
PBI	120 DAYS							
ACN:H_2O Extract	0.622	87.6	0.021	46.7	0.299	90.3	0.021	46.7
0.1 N KOH Extract	0.031	4.4	0.004	8.9	0.012	3.6	0.004	8.9
24% KOH Extract	0.045	6.3	0.014	31.1	0.018	5.4	0.014	31.1
72% H_2SO_4 Extract	0.007	1.0						
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	0	0.0	–	–	0.000	0.0
Aqueous Phase	–	–	0.018	40.0	–	–	0.016	35.6
PES	0.005	0.7	0.006	13.3	0.002	0.6	0.006	13.3
Total	0.710		0.045		0.331	99.9	0.045	
PBI	390 DAYS [a]							
ACN:H_2O Extract	0.119	89.5	0.030	60.0	0.331	97.6	0.030	60.0
0.1 N KOH Extract	0.004	3.0	0.004	8.0	0.002	0.6	0.004	8.0
24% KOH Extract	0.009	6.8	0.013	26.0	0.005	1.5	0.013	26.0
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	0.002	1.5	0.003	6.0	–	–	–	–
Aqueous Phase	0.011	8.3	0.014	28.0	–	–	–	–
PES	0.001	0.8	0.003	6.0	0.001	0.3	0.003	6.0
Total	0.133		0.050		0.339		0.050	

[a] 390-day lettuce samples because of crop failure of 360-day lettuce samples.

Table 46 Extraction summary for wheat forage and straw after soil treatment with [^{14}C]fluensulfone

Crop	Wheat							
Matrix	Forage				Straw			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	15.594	94.1	2.240	88.5	15.626	84.2	1.035	53.5
0.1 N KOH Extract	0.300	1.8	0.073	2.9	0.906	4.9	0.195	10.1
24% KOH Extract	0.538	3.2	0.184	7.3	1.443	7.8	0.350	18.1
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	–	–	0.507	2.7	0.079	4.1
Aqueous Phase	–	–	–	–	1.842	9.9	0.466	24.1
72% H_2SO_4 Extract	–	–	–	–	0.441	2.4	0.283	14.6
PES	0.147	0.9	0.033	1.3	0.153	0.8	0.072	3.7
Total	16.579		2.530		18.569		1.935	
PBI	120 DAYS							
ACN:H_2O Extract	2.809	94.8	0.642	90.0	2.966	84.3	0.195	64.4
0.1 N KOH Extract	0.079	2.7	0.024	3.4	0.094	2.7	0.041	13.5

Crop	Wheat							
Matrix	Forage				Straw			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
24% KOH Extract	0.058	2.0	0.038	5.3	0.331	9.4	0.042	13.9
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	0.005	0.7	0.081	NR	0.013	NR
Aqueous Phase	–	–	0.057	8.0	0.344	NR	0.070	NR
72% H_2SO_4 Extract	0.012	0.4	0.007	1.0	0.126	3.6	0.025	8.3
PES	0.005	0.2	0.002	0.3	0.126	3.6	0.025	8.3
Total	2.963		0.713		3.517		0.303	
PBI	360 DAYS							
ACN:H_2O Extract	3.157	94.9	0.039	65.0	6.051	91.2	0.102	61.8
0.1 N KOH Extract	–	–	0.003	5.0	0.259	3.9	0.011	6.7
24% KOH Extract	–	–	0.014	23.3	0.229	3.5	0.032	19.4
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	–	–	0.094	1.4	0.010	6.1
Aqueous Phase	–	–	–	–	0.394	5.9	0.033	20.0
PES	0.169	5.1	0.004	6.7	0.097	1.5	0.020	12.1
Total	3.326		0.060		6.636		0.165	

Table 47 Extraction summary for wheat hay and grain after soil treatment with [^{14}C]fluensulfone

Crop	Wheat							
Matrix	Hay				Grain			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	18.891	70.0	2.127	47.3	0.263	73.3	0.109	63.7
0.1 N KOH Extract	5.321	19.7	1.478	32.8	0.034	9.6	–	–
24% KOH Extract	2.224	8.2	0.741	16.5	–	–	–	–
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	1.177	4.4	0.249	5.5	0.003	0.8	–	–
Aqueous Phase	6.368	23.6	1.970	43.8	0.059	16.6	–	–
72% H_2SO_4 Extract	0.479	1.8	–	–	–	–	–	–
PES	0.089	0.3	0.154	3.4	–	–		
Total	27.004		4.500		0.359		0.173	
PBI	120 DAYS							
ACN:H_2O Extract	7.185	76.5	0.225	60.3	0.247	83.4	0.023	39.0
0.1 N KOH Extract	1.288	13.7	0.060	16.1	0.017	5.7	0.006	10.2
24% KOH Extract	0.715	7.6	0.068	18.2	0.003	1.0	0.001	1.7
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	0.282	3.0	0.009	2.4	–	–	–	–
Aqueous Phase	1.721	18.3	0.119	31.9	–	–	–	–
72% H_2SO_4 Extract	0.209	2.2	0.020	5.4	–	–	–	–
PES	0.209	2.2	0.020	5.4	0.029	9.8	0.029	49.2
Total	9.397		0.373		0.296		0.059	
PBI	360 DAYS							
ACN:H_2O Extract	7.768	71.7	0.070	54.7	0.260	76.0	0.013	34.2
0.1 N KOH Extract	1.166	10.8	0.011	8.6	0.022	6.4	0.006	15.8
24% KOH Extract	1.230	11.4	0.026	20.3	–	–	–	–
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	0.594	5.5	0.001	8.6	0.008	2.3	–	–
Aqueous Phase	1.802	16.6	0.026	20.3	0.014	4.1	–	–
PES	0.671	6.2	0.021	16.4	0.060	17.5	0.019	50.0
Total	10.835		0.128		0.342		0.038	

Table 48 Summary of [Th-^{14}C]fluensulfone labelled residues in radish foliage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	5.263	100.0	1.756	100.0	2.860	100.0
Solvent Extractable	5.166	98.2	1.709	97.3	2.842	99.4
Fluensulfone	0.010	0.2	–	–	–	–
Thiazole Sulfonic Acid	4.726	89.8	1.624	92.5	2.558	89.4
M1—Form of TSA	0.113	2.2	0.073	4.2	–	–
M3—Form of TSA	0.034	0.6	–	–	–	–
Unresolved	0.258	4.9	0.012	0.7	0.283	9.9

Table 49 Summary of [Th-^{14}C]fluensulfone labelled residues in radish roots

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.793	100.0	0.437	100.0	0.379	100.0
Solvent Extractable	0.723	91.2	0.382	87.4	0.365	96.3
Thiazole Sulfonic Acid	0.687	86.6	0.355	81.2	0.341	90.0
M1—Form of TSA	–	–	0.004	0.9	–	–
M3—Form of TSA	0.004	0.5	0.001	0.2	0.004	1.1
Unresolved	0.020	2.5	0.016	4.2	0.019	5.0

M1: This fraction consists of two compounds with the major part of this identified a salt of TSA.

M3: This polar radioactive fraction was always observed as a possible artifact due to the non-retention of TSA.

Alkaline and acid digestion released additional small amounts of radiolabelled compounds.

Table 50 Summary of [Bu-^{14}C]fluensulfone labelled residues in radish foliage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.479	100.0	0.467	100.0	0.038	100.0
Solvent Extractable	0.452	94.4	0.436	93.4	0.031	81.6
Fluensulfone	0.015	3.1	0.024	5.1	0.001	3.0
Butene Sulfonic Acid	0.315	65.8	0.328	70.2	–	–
F1-F2—Form of BSA	0.016	3.4	0.002	0.4	0.002	5.1
F4—Form of BSA	0.017	3.5	–	–	–	–
F5	0.005	1.0	0.015	3.2	0.001	3.6
F6	0.001	0.2	–	–	0.002	5.3
F7	–	–	–	–	0.005	13.2
F9	–	–	–	–	0.001	3.2
Unresolved	0.059	12.3	0.068	14.6	0.013	34.2

Table 51 Summary of [Bu-^{14}C]fluensulfone labelled residues in radish roots

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.146	100.0	0.104	100.0	0.012	100.0
Solvent Extractable	0.126	86.3	0.079	76.0	0.006	50.0
Fluensulfone	0.002	1.5	–	–	–	–
Butene Sulfonic Acid	0.058	40.0	0.041	39.4	–	–
F1 - F2—Form of BSA	0.009	6.2	0.002	2.3	0.001	8.3
F5	0.007	4.8	0.005	4.5	–	–
F7	0.006	3.8	–	–	–	–
Unresolved	0.034	23.3	0.025	24.0	0.005	41.7

Table 52 Summary of [Th-^{14}C]fluensulfone labelled residues in immature lettuce

	30-Day PBI		120-Day PBI		390-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.647	100.0	0.710	100.0	0.133	100.0
Solvent Extractable	0.495	76.5	0.622	87.6	0.119	89.5
Fluensulfone	0.005	0.8	0.004	0.6	–	–
Thiazole Sulfonic Acid	0.183	28.3	0.401	56.5	0.086	64.7
M1—Form of TSA	0.122	18.9	0.113	15.9	0.013	9.8
M2—Form of TSA	–	–	0.009	1.3	–	–
M3—Form of TSA	0.007	1.1	0.004	0.6	0.003	2.3
Unresolved	0.179	27.7	0.091	12.8	0.016	12.0

Table 53 Summary of [Th-^{14}C]fluensulfone labelled residues in mature lettuce

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.565	100.0	0.331	100.0	0.339	100.0
Solvent Extractable	0.494	87.4	0.299	90.3	0.331	97.6
Fluensulfone	0.006	1.1	–	–	–	–
Thiazole Sulfonic Acid	0.237	41.9	0.184	55.6	0.279	82.3
M1—Form of TSA	0.113	20.0	0.086	26.0	0.004	1.2
M3—Form of TSA	0.002	0.4	0.004	1.2	–	–
Unresolved	0.134	23.7	0.025	7.6	0.046	13.6

M1: This fraction consists of two compounds with the major part of this identified as a salt of TSA.

M3: This polar radioactive fraction was always observed as a possible artifact due to the non-retention of TSA.

Alkaline & acid digestion: Unresolved metabolites were released especially with 24% KOH. A major component appeared to be TSA.

Table 54 Summary of [Bu-^{14}C]fluensulfone labelled residues in immature lettuce

	30-Day PBI		120-Day PBI		390-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.311	100.0	0.045	100.0	0.050	100.0
Solvent Extractable	0.221	71.1	0.021	46.7	0.030	60.0
Fluensulfone	0.016	5.1	–	–	0.002	4.0
Butene Sulfonic Acid	0.004	1.2	0.001	2.2	–	–
F1-F2—Form of BSA	0.006	1.9	0.006	13.3	0.005	10.0
F4—Form of BSA	< 0.001	0.1	0.002	4.4	–	–
F5	0.002	0.5	–	–	–	–
F6	0.003	1.2	–	–	–	–
F7	0.002	0.6	0.001	1.3	0.001	2.0
F9	0.010	3.2	0.001	2.2	–	–
F10	< 0.001	0.1	–	–	–	–
Unresolved	0.176	56.6	0.009	20.0	0.019	38.0

Table 55 Summary of [Bu-^{14}C]fluensulfone labelled residues in mature lettuce

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.204	100.0	0.045	100.0	0.017	100.0
Solvent Extractable	0.137	67.2	0.027	60.0	0.008	47.1
Fluensulfone	0.004	2.0	–	–	–	–
Butene Sulfonic Acid	0.018	8.8	–	–	–	–
F1-F2—Form of BSA	0.011	5.4	0.016	35.6	0.002	11.8

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
F5	0.001	0.6	–	–	–	–
Unresolved	0.100	49.0	0.010	21.9	0.006	35.3

Table 56 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat forage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	16.579	100.0	2.963	100.0	3.326	100.0
Solvent Extractable	15.594	94.1	2.809	94.8	3.157	94.9
Thiazole Sulfonic Acid	12.241	73.8	2.254	76.0	2.737	82.3
M1—Form of TSA	0.521	3.1	0.104	3.5	0.011	0.3
M3—Form of TSA	0.147	0.9	–	–	0.036	1.1
Unresolved	2.237	13.5	0.449	15.2	0.376	11.3

Table 57 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat hay

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	27.004	100.0	9.397	100.0	10.835	100.0
Solvent Extractable	18.891	70.0	7.185	76.5	7.768	71.7
Thiazole Sulfonic Acid	15.571	57.7	6.221	66.2	5.771	53.3
M1—Form of TSA	0.496	1.8	0.227	2.4	0.084	0.8
M3—Form of TSA	0.413	1.5	0.167	1.8	0.542	5.0
Unresolved	2.348	8.7	0.498	5.3	1.313	12.1

Table 58 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat grain

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.359	100.0	0.296	100.0	0.342	100.0
Solvent Extractable	0.263	73.9	0.247	83.4	0.260	76.0
Thiazole Sulfonic Acid	0.120	33.4	0.171	57.8	0.195	57.0
M1—Form of TSA	0.047	13.1	0.011	3.7	0.029	8.5
M3—Form of TSA	0.018	5.0	0.009	3.0	0.009	2.6
Unresolved	0.078	21.7	0.056	18.9	0.027	7.9

Table 59 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat straw

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	18.569	100.0	3.517	100.0	6.636	100.0
Solvent Extractable	15.626	84.2	2.966	84.3	6.051	91.2
Thiazole Sulfonic Acid	10.712	57.7	2.196	62.4	5.060	76.3
M1—Form of TSA	0.364	2.0	0.031	0.9	0.056	0.8
M3—Form of TSA	0.273	1.5	–	–	0.401	6.0
Unresolved	4.268	23.0	0.727	20.7	0.484	7.3

M1 & M3: Fraction not confirmed by TLC analysis leading to the suggestion to be a chromatographic artifact of TSA. Alkaline and acid digestion, especially with 24% KOH, liberated several, unresolved metabolites that could not be identified. A major component appeared to be TSA.

Table 60 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat forage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	2.530	100.0	0.713	100.0	0.060	100.0
Solvent Extractable	2.240	88.5	0.642	90.0	0.039	65.0
Fluensulfone	0.028	1.1	0.021	2.9	–	–
Butene Sulfonic Acid	1.377	54.4	0.427	59.9	0.002	3.2
F1-F2—Form of BSA	0.090	3.6	0.026	3.6	0.009	15.0
F4—Form of BSA	0.020	7.9	0.016	2.2	–	–
F5	0.069	2.7	0.038	5.3	0.001	1.7
F6	0.035	1.4	–	–	–	–
F7	0.004	0.1	–	–	–	–
F9	0.041	1.6	0.015	2.1	–	–
F10	0.019	0.8	–	–	–	–
Unresolved	0.374	14.8	0.066	9.3	0.024	40.0

Table 61 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat hay

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	4.500	100.0	0.373	100.0	0.128	100.0
Solvent Extractable	2.127	47.3	0.225	60.3	0.070	54.7
Fluensulfone	0.016	0.4	0.004	1.1	–	–
Butene Sulfonic Acid	1.223	27.2	0.095	25.5	–	–
F1-F2—Form of BSA	0.059	1.3	0.033	8.8	0.021	16.4
F4—Form of BSA	0.050	1.1	0.006	1.7	0.001	0.8
F5	0.077	1.7	0.006	1.6	0.002	1.4
F6	–	–	–	–	0.001	0.6
F7	–	–	–	–	0.001	0.8
F9	–	–	0.003	0.8	0.002	1.6
F10	–	–	–	–	–	–
Unresolved	0.700	15.6	0.064	17.2	0.037	28.9

Table 62 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat grain

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.173	100.0	0.059	100.0	0.038	100.0
Solvent extractable	0.109	63.0	0.023	39.0	0.013	34.2
F1-F2—Form of BSA	0.007	4.0	0.011	18.6	0.004	10.5
unresolved	0.102	59.0	0.012	20.3	0.009	23.7

Table 63 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat straw

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	1.935	100.0	0.303	100.0	0.165	100.0
Solvent Extractable	1.035	53.5	0.195	64.4	0.102	61.8
Fluensulfone	0.004	0.2	–	–	–	–
Butene Sulfonic Acid	0.272	14.1	0.031	10.2	0.012	7.0
F1-F2—Form of BSA	0.189	9.8	0.095	31.4	0.016	9.7
F5	0.007	0.4	–	–	0.002	1.0
F9	0.007	0.3	–	–	0.002	1.0
Unresolved	0.546	28.2	0.068	22.4	0.069	41.8

F3: Suggested to be BSA. Due to matrix effects the retention time of BSA is changing considerably leading to chromatographic artefacts.

F4 & F5: The HPLC-MS analysis of these fractions gave a high molecular weight which suggests that it is possibly a natural product.

Field rotational crop studies

No field rotational crop studies were provided.

Field dissipation studies

No field dissipation studies were provided.

RESIDUE ANALYSIS

Summary of analytical methods

Methods for the analysis of fluensulfone and its breakdown products BSA, MeS, and TSA are generally the same for plant, animal, and soil matrices, though there are some differences in the extraction of BSA and TSA in eggs and milk and in the clean-up steps for fatty samples. The methods are summarized in Table 64.

Table 64 Overview of the analytical methods submitted for fluensulfone and its major metabolites

Method ID (Report)	Matrix	Analyte	Extraction	Clean-up	Separation/ Analysis/LOQ
1997W (R-23334 and R-28495) Equivalent to 2061W	Plant commodities	Fluensulfone + MeS	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS Fluensulfone m/z 292 $[M+H]^+ \rightarrow$ 166 (q) m/z 292 → 89 (c) m/z 292 → 59 (c) LOQ: 0.01 mg/kg MeS m/z 198 $[M+H]^+ \rightarrow$ 120 (q) m/z 198 → 122 (q) LOQ: 0.01 mg/kg
		BSA + TSA	ACN+H_2O (1+1, v/v)	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^- \rightarrow$ 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^- \rightarrow$ 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg
10M04006-01-VMPL (R-28495)	Plant commodities	MeS	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS m/z 198 $[M+H]^+ \rightarrow$ 120 (q) m/z 198 → 122 (q) LOQ: 0.01 mg/kg
11M03036-01-VMPL (R-23489)	Plant commodities	Fluensulfone	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS m/z 292 $[M+H]^+ \rightarrow$ 166 (q) m/z 292 → 89 (c) m/z 292 → 59 (c) LOQ: 0.01 mg/kg
		MeS	ACN+H_2O (1+1, v/v)	Orange: filtration Wheat grain and peanut:	LC-MS/MS m/z 198 $[M+H]^+ \rightarrow$ 120 (q) m/z 198 → 122 (q) LOQ: 0.01 mg/kg

Method ID (Report)	Matrix	Analyte	Extraction	Clean-up	Separation/ Analysis/LOQ
				partition against hexane + filtration	
		BSA + TSA	ACN+H_2O (1+1, v/v)	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^-$ → 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^-$ → 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg
11M03036-01-VMAT (R-28512)	Animal commodities	Fluensulfone + MeS	ACN+H_2O (1+1, v/v)	Fat: filtration All others: partition against hexane	LC-MS/MS Fluensulfone m/z 292 $[M+H]^+$ → 166 (q) m/z 292 → 89 (c) LOQ: 0.01 mg/kg MeS m/z 198 $[M+H]^+$ → 120 (q) m/z 198 → 125 (c) LOQ: 0.01 mg/kg
		BSA + TSA	Liver, kidney, meat, fat: ACN+H_2O (1+1, v/v) Eggs, milk: ACN	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^-$ → 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^-$ → 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg
2049W (R-23339)	Soils	Fluensulfone + MeS	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS Fluensulfone m/z 292 $[M+H]^+$ → 166 (q) m/z 292 → 89 (c) LOQ: 0.01 mg/kg MeS m/z 198 $[M+H]^+$ → 135 (q) m/z 198 → 93 (c) LOQ: 0.01 mg/kg
		BSA + TSA	ACN+H_2O (1+1, v/v)	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^-$ → 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^-$ → 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg

Plant materials

For plant matrices, Method 1997W (equivalent to Method 2061W) has been developed as a suitable enforcement method by J. Marin (2010, Report R-23334) for fluensulfone, BSA, and TSA, and expanded by A. Witte (2011, Report R-28495) to include MeS. The method underwent independent validation for all four analytes by R. Bacher (2011, Report R-27478).

Residues are extracted from 10 g of sample matrix using ACN:H_2O (1:1, v/v, 50 mL) by shaking for five minutes followed by centrifugation. The extract is then split, with one aliquot for

analysis of fluensulfone/MeS and a second aliquot for analysis of BSA/TSA. Quantification of all residues is by comparison with external, matrix-matched standards.

For fluensulfone (all matrices) and MeS (non-grain/non-oily matrices), an aliquot of the extract is filtered (0.45 µm) and analysed, without further clean-up, by LC-MS/MS in positive ion spray mode. For MeS in grain and oily matrices, the extract is salted out with NaCl; the separated ACN phase is dried with $MgSO_4$ and an aliquot is partitioned against hexane to remove co-extracted material. The ACN phase is collected, evaporated to dryness, and the residues are reconstituted in ACN:H_2O (1:1, v/v). The resulting extract is filtered (0.45 µm) and analysed by LC-MS/MS in positive ion spray mode. Chromatography for all extracts is done on a reverse-phase C_{-18} column maintained at 45 °C using a gradient mobile phase that transitions from 0.1% formic acid in ACN (95%) + 0.1% formic acid in H_2O (5%) to 0.1% formic acid in H_2O (100%). Ion transitions $[M+H]^+$ for fluensulfone are *m/z* 292 → 166 for quantitation (q), *m/z* 292 → 89 for confirmation (c), and *m/z* 292 → 59 (c). Ion transitions for MeS are *m/z* 198 → 120 (q) and the corresponding chlorine isotope transition (*m/z* 200 → 122).

For BSA and TSA (all matrices), a 6 mL aliquot of the initial extract is concentrated to 3 mL and cleaned-up on a C_{-18} SPE cartridge. Eluate from the cartridge is brought to volume and analysed by LC-MS/MS in negative ion mode. Chromatography is by reverse-phase C_{-18} column maintained at 45 °C using a gradient mobile phase that transitions from 0.05% formic acid in ACN (95%) + 0.05% formic acid in H_2O (5%) to 0.05% formic acid in H_2O (100%). Ion transitions $[M-H]^-$ for BSA are *m/z* 189 → 81 (q) and *m/z* 189 → 80 (c). Ion transitions for TSA are *m/z* 198 → 89 (q) and *m/z* 198 → 118).

Linearity data were provided and showed linear responses ($R^2 \geq 0.992$ and generally > 0.998) from 0.2–20 ng/mL. In a few studies, linearity was demonstrated over a broader range, including up to 100 ng/mL. Accuracy and precision data, in the form of spike and recovery studies, were provided for cucumber, lemon, melon, orange flesh, peanut, pepper, tomato and wheat grain. Samples were spiked at either 0.01 or 1 mg/kg of fluensulfone, BSA, MeS, or TSA (separately). Mean recoveries for each analyte at each spiking level and for each matrix were within the generally accepted range of 70–120%. Of the 860 method validation analyses, ten had recoveries outside of the generally accepted range of 70–120%: 53% and 54% for TSA in peanut, 174% for BSA in wheat grain, and seven recoveries ranging from 121% to 170% for fluensulfone, MeS, or TSA in orange flesh or lemon. In all cases, relative standard deviations were ≤ 20%.

Testing of fluensulfone and the two sulfonic acid metabolites, BSA and TSA, through the FDA PAM multiresidue method protocols was conducted by T. Ballard (2012, Report R-29565) for non-fatty foods. The compounds showed poor sensitivity, poor recovery, and/or poor chromatography. Overall, the results indicate that the FDA PAM multiresidue protocols are not suitable for the detection or enforcement of fluensulfone, BSA, or TSA residues in non-fatty foods.

Animal materials

A residue analytical method for the analysis of fluensulfone and its BSA, MeS, and TSA metabolites in animal matrices has been developed by Witte (2011, Report R-28512). It is identical to the method for those analytes in plant matrices described above, with the exception of the extraction of BSA and TSA from eggs and milk. For those matrices, extraction is accomplished with ACN (neat). The method was successfully validated by R. Bacher (2012, Report R-29562).

As with the plant method, extracts (except eggs and milk) are split for separate analysis of fluensulfone and MeS or BSA and TSA. For fluensulfone/MeS, the only clean-up is filtration whereas for BSA and TSA, there is clean-up by C_{-18} SPE and filtration. The LC-MS/MS conditions and ions are the same as described above for plants. The method showed linear response from 0.2–20 ng/mL for fluensulfone and MeS, and from 0.2–15 ng/mL for BSA and TSA. Recoveries from 900 spike-and-recovery analyses for all three analytes ranged from 71–109%, with the exception of four analyses, all for fluensulfone: 122% in pork meat, 154% in kidney, and 164% for liver, and egg.

Soil

A residue analytical method for the analysis of fluensulfone and its BSA, MeS, and TSA metabolites in animal matrices has been developed by Marin (2010, Report R-23339, Method 2049W). It is identical to the method for those analytes in plant matrices described above. The method was successfully validated by R. Barker (2012, Report R-29564).

As with the plant method, extracts are split for separate analysis of fluensulfone and MeS or BSA and TSA. For fluensulfone/MeS, the only clean-up is filtration whereas for BSA and TSA, there is clean-up by C_{-18} SPE and filtration. The LC-MS/MS conditions and ions are the same as described above for plants.

Mean recoveries ranged from 78 to 114% for all analyses, with relative standard deviations of < 12%.

Stability of residues in stored samples

The stability of fluensulfone, BSA, and TSA in frozen storage has been investigated in tomato, pepper (Korpalski, S. 2011, 09-01858), cucumber and melon (Korpalski, S. 2011, 09-01859). In addition, the stability of those analytes and MeS was investigated in frozen, stored tomato puree and paste (Jones, G.L. 2011, R-23487). No dissipation of any analyte was observed during the storage periods for the various matrices. Stability was demonstrated in tomato raw agricultural commodity (RAC) for at least 469 days (ca. 15 months) and in tomato processed commodities for at least 181 days (ca. 6 months). For pepper, cucumber, and melon, residues were stable for at least 488 days (ca. 16 months).

Table 65 Storage Stability of fluensulfone, TSA and BSA in cucumber

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	102, 90, 112	–
	91 / 3		100, 106	104, 97, 101
	266 / 9		84, 82	92, 104, 98
	488 / 16		79, 74	88, 86, 92
TSA	0 / 0	0.10	99, 97, 90	–
	91 / 3		101, 97	104, 105, 105
	267 / 9		110, 110	109, 110, 115
	488 / 16		94, 98	97, 100, 102
BSA	0 / 0	0.10	95, 104, 93	–
	91 / 3		100, 97	97, 95, 96
	267 / 9		110, 108	115, 118, 119
	488 / 16		98, 96	96, 105, 105

Table 66 Storage stability of fluensulfone, TSA and BSA in melon

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	79, 96, 77	–
	91 / 3		100, 103	101, 91, 106
	266 / 9		84, 76	74, 96, 95
	488 / 16		77, 79	91, 98, 98
TSA	0 / 0	0.10	85, 92, 89	–
	91 / 3		93, 97	90, 95, 97
	267 / 9		103, 103	110, 108, 113
	488 / 16		95, 94	89, 93, 89
BSA	0 / 0	0.10	83, 99, 93	–
	91 / 3		81, 90	79, 85, 89
	267 / 9		100, 103	115, 117, 116
	488 / 16		89, 93	93, 99, 94

Table 67 Storage stability of fluensulfone, TSA and BSA in pepper

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	91, 80, 89	–
	95 / 3		116, 117	113, 116, 119
	263 / 8.5		103, 107	102, 108, 109
	488 / 16		90, 94	96, 98, 106
TSA	0 / 0	0.10	85, 77, 81	–
	95 / 3		103, 101	105, 88, 95
	263 / 8.5		95, 100	94, 108, 101
	488 / 16		92, 89	85, 94, 98
BSA	0 / 0	0.10	76, 74, 78	–
	95 / 3		98, 110	97, 87, 99
	263 / 8.5		94, 102	102, 103, 102
	488 / 16		89, 94	102, 106, 107

Table 68 Storage stability of fluensulfone, TSA and BSA in tomato

Analyte	Storage Interval	Spiking	Percent of Nominal Spiking Level

	days / months	Level (mg/kg)	Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	85, 117, 105	–
	92 / 3		97, 94	97, 87, 98
	244 / 8		112, 108	109, 108, 108
	469 / 15		78,98	96, 99, 100
TSA	0 / 0	0.10	101, 89, 97	–
	92 / 3		88, 84	91, 90, 91
	244 / 8		114, 95	102, 92, 108
	469 / 15		90, 89	94, 95, 93
BSA	0 / 0	0.10	96, 95, 99	–
	92 / 3		88, 89	87, 81, 84
	244 / 8		105, 95	96, 86, 104
	469 / 15		93, 97	96, 106, 98

Table 69 Storage stability of fluensulfone, TSA, MES and BSA in tomato puree

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	27 / 1	0.10	104, 107	103, 108
	89 / 3		101, 100	98, 86
	181 / 6		80, 84	73, 75
TSA	27 / 1	0.10	80, 74	80, 78
	89 / 3		81, 81	81, 88
	181 / 6		72, 73	79, 81
MES	27 / 1	0.10	88, 88	85, 90
	89 / 3		93, 98	100, 82
	181 / 6		89, 86	88, 87
BSA	27 / 1	0.10	89, 98	93, 98
	89 / 3		93, 95	93, 94
	181 / 6		92, 95	98, 99

Table 70 Storage stability of fluensulfone, TSA, MES and BSA in tomato paste

Analyte	Storage Interval days / months	Spiked Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	90 / 3	0.10	97, 87	79, 74
	181 / 6		94, 92	83, 73
TSA	90 / 3	0.10	62, 63	65, 65
	181 / 6		63, 63	67, 69
MES	90 / 3	0.10	92, 88	89, 86
	181 / 6		82, 88	89, 88
BSA	90 / 3	0.10	73, 80	87, 85
	181 / 6		85, 84	89, 93

USE PATTERN

Table 71 Good agricultural practices (GAPs) proposed for fluensulfone [a]

Crop and/ or Situation	Pests or Group of Pests Controlled	Application Method Kind	Growth Stage & Season	No.	Interval Between Applications (min)	Rate (kg ai/ha, min–max)	PHI (days)
U.S.A Registration							
Cucurbit	Root-knot,	Drip irrigation,	Pre-planting	1	N/A	1.92–2.8	N/A

Crop and/ or Situation	Pests or Group of Pests Controlled	Application Method Kind	Growth Stage & Season	No.	Interval Between Applications (min)	Rate (kg ai/ha, min–max)	PHI (days)
vegetables & fruiting vegetables	root-lesion and cyst nematodes	Band application, Broadcast spray	(minimum of 7 days before transplanting) [b]				

[a] Representative formulation is an EC containing 480 g/L (4 lb/gal) of fluensulfone.

[b] Only outdoor uses are permitted.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received data from supervised residue trials conducted on cucumber, summer squash, cantaloupe, tomato, and pepper conducted in the USA and Canada. For all samples, analyses were conducted for fluensulfone, BSA, and TSA, and analysis of MeS was conducted for at least some samples from each crop. The reports included method validation data, as recoveries from spiked samples at levels reflecting those observed in the field trial samples; dates from critical events during the study, including application, harvest, storage, and analysis; as well as detailed information on the field site and treatment parameters. Analytical reports were sufficiently detailed and included example chromatograms and example calculations. Samples were analysed by Method 1997W (equivalent to Method 2061W) described above. The results are supported by concurrent recoveries ranging, on average for each analyte and crop, from 81–120% for all commodity × analyte combinations except for fluensulfone in dry tomato pomace, which averaged 131% in one study. Samples were stored, frozen, for the following durations: cucumber = 10 months, squash = 10 months, melons = 9 months, pepper = 7 months, and tomato = 7 months. The storage durations are less than or equal to those for which residues have been demonstrated to be stable.

The field trial study designs included control plots. All measured residues from control plots were < 0.01 mg/kg (i.e., < LOQ) and are not included in the summary tables in this evaluation.

Supervised trials for fluensulfone:

Commodity	Crop	Table
Fruiting vegetable, cucurbit	Cucumber (VC 0424)	Table 72
Fruiting vegetable, cucurbit	Summer squash (VC 0431)	Table 73
Fruiting vegetable, cucurbit	Cantaloupe/muskmelon (VC 4199/VC 4239)	Table 74, 75
Fruiting vegetable, other than cucurbit	Pepper (VO 0051	Table 76
Fruiting vegetable, other than cucurbit	Tomato (VO 0448)	Table 77

Fruiting Vegetables, Cucurbits

Cucumber

Table 72 Residues of fluensulfone, BSA, MeS, and TSA in cucumber following pre-plant treatment.

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Montezuma, Georgia, USA 2010 [Speedway]	4.01	2087	3 days pre-plantin g	drip irrigation	46	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.039, 0.058 (0.049)
(09-01859)					49	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.056, 0.065 (0.061)
					53	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.052, 0.049 (0.051)
					56	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.050, 0.085 (0.068)
					60	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.039, 0.035 (0.037)
Clermont, Florida, USA 2009 [Marketmore 76]	4.00	2083	3 days pre-plantin g	drip irrigation	70	< 0.01, < 0.01 (< 0.01)	0.012, 0.019 (0.016)	n.a.	0.020, 0.035 (0.028)
(09-01859)					73	< 0.01, < 0.01 (< 0.01)	0.013, < 0.01 (0.011)	n.a.	0.029, 0.014 (0.022)
					77	< 0.01, < 0.01 (< 0.01)	0.012, < 0.01 (0.011)	n.a.	0.028, 0.014 (0.021)
					80	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.012 (0.011)	n.a.	0.013, 0.026 (0.020)
					84	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.022 (0.016)	n.a.	0.020, 0.037 (0.029)
Fresno, California, USA 2009 [Straight Eight]	4.00	2083	3 days pre-plantin g	drip irrigation	78	< 0.01, < 0.01 (< 0.01)	0.048, 0.071 (0.060)	n.a.	0.063, 0.090 (0.077)
(09-01859)					81	< 0.01, < 0.01 (< 0.01)	0.030, 0.032 (0.031)	n.a.	0.050, 0.038 (0.044)
					85	< 0.01, < 0.01 (< 0.01)	0.033, 0.032 (0.033)	n.a.	0.056, 0.046 (0.051)
					88	< 0.01, < 0.01 (< 0.01)	0.035, 0.028 (0.032)	n.a.	0.040, 0.040 (0.040)
					92	< 0.01,	0.034, 0.018	n.a.	0.052, 0.044

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
						< 0.01 (< 0.01)	(0.026)		(0.048)
Visalia, California, USA 2010 [Poinsett 76] (AA100708)	4.09	379	7 d pre-plantin g	BCS	70	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
	4.00	9000	7 d pre-plantin g	drip irrigation	70	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Hobe Sound, Florida, USA 2010 [Impact] (AA100708)	3.87	222	7 d pre-plantin g	BCS	45	< 0.01, < 0.01 (< 0.01)	0.076, 0.064 (0.070)	0.028, 0.029 (0.029)	0.048, 0.040 (0.044)
Athens, Georgia, USA 2010 [Burpless Hybrid] (AA100708)	4.05	361	7 d pre-plantin g	BCS	71	< 0.01, < 0.01 (< 0.01)	0.010, 0.010 (0.010)	0.011, 0.011 (0.011)	0.081, 0.084 (0.083)
Seven Springs, North Carolina, USA 2010 [Ashley] (AA100708)	4.10	358	7 d pre-plantin g	BCS	41	< 0.01, < 0.01 (< 0.01)	0.085, 0.215 (0.150)	0.021, 0.024 (0.023)	0.408, 0.524 (0.47)
	4.00	9000	7 d pre-plantin g	drip irrigation	41	< 0.01, < 0.01 (< 0.01)	**0.353**, 0.084 (0.22)	0.035, 0.042 (0.039)	0.718, 0.500 (0.61)
Raymondville, Texas, USA 2010 [Sweet Slice] (AA100708)	3.72	261	7 d pre-plantin g	BCS	46	< 0.01, < 0.01 (< 0.01)	0.176, 0.164 (0.17)	0.079, 0.071 (0.075)	0.522, 0.507 (0.52)
Thorndale, Ontario, Canada 2010 [Cross Country] (AA100708)	3.81	381	8 d pre-plantin g	BCS	50	< 0.01, < 0.01 (< 0.01)	0.045, 0.081 (0.063)	0.061, 0.075 (0.068)	0.198, 0.258 (0.23)
Portage la Prairie, Manitoba, Canada 2010 [Slicing] (AA100708)	4.11	359	7 d pre-plantin g	BCS	73	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.011 (0.010)	< 0.01, < 0.01 (< 0.01)	0.058, 0.070 (0.064)

Applic. Type BCS = broadcast spray

Residue n.a. = Not analysed

Summer squash

Table 73 Residues of fluensulfone, BSA, MeS, and TSA in summer squash following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Porterville, California, USA 2010 [Dark Green Zucchini] (AA100708)	3.82	286	7 d pre-plantin g	BCS	49	< 0.01, < 0.01 (< 0.01)	0.014, 0.010 (0.012)	< 0.01, < 0.01 (< 0.01)	0.040, 0.028 (0.034)
	4.00	9000	7 d pre-plantin g	drip irrigation	49	< 0.01, < 0.01 (< 0.01)	0.062, 0.058 (0.060)	< 0.01, < 0.01 (< 0.01)	0.127, 0.079 (0.10)
Dover, Florida, USA 2010 [Enterprise] (AA100708)	4.01	250	7 d pre-plantin g	BCS	36	< 0.01, < 0.01 (< 0.01)	0.086, 0.078 (0.082)	< 0.01, < 0.01 (< 0.01)	0.117, 0.106 (0.11)
Seven Springs, North Carolina, USA 2010 [Early Prolific Straight neck] (AA100708)	4.02	352	7 d pre-plantin g	BCS	41	< 0.01, < 0.01 (< 0.01)	0.206, 0.165 (0.19)	0.033, 0.037 (0.035)	0.715, 0.701 (0.71)
Hinton, Oklahoma, USA 2010 [Enterprise] (AA100708)	4.02	256	6 d pre-plantin g	BCS	61	< 0.01, < 0.01 (< 0.01)	0.196, 0.231 (0.21)	0.023, 0.018 (0.021)	0.366, 0.563 (0.46)
Ephrata, Washington, USA 2010 [Aristocrat] (AA100708)	4.14	389	7 d pre-plantin g	BCS	62	< 0.01, < 0.01 (< 0.01)	**0.256**, 0.237 (0.25)	0.050, 0.045 (0.048)	0.267, 0.237 (0.25)
Berwick, Nova Scotia, Canada 2010 [Payroll] (AA100708)	4.07	363	7 d pre-plantin g	BCS	38	< 0.01, < 0.01 (< 0.01)	0.222, 0.169 (0.20)	0.016, 0.011 (0.014)	0.292, 0.253 (0.27)
Branchton, Ontario, Canada 2010 [Senator] (AA100708)	3.89	241	6 d pre-plantin g	BCS	45	< 0.01, 0.017 (< 0.013)	0.065, 0.035 (0.00)	0.013, 0.010 (0.012)	0.063, 0.051 (0.057)
	4.00	9000	6 d pre-plantin g	drip irrigation	45	< 0.01, < 0.01 (< 0.01)	0.029, 0.060 (0.045)	< 0.01, < 0.01 (< 0.01)	0.038, 0.061 (0.050)
Elm Creek, Manitoba,	3.80	286	7 d pre-plantin	BCS	71	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01	< 0.01, < 0.01	0.036, 0.034 (0.035)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
Canada 2010 [Zucchini] (AA100708)			g				(< 0.01)	(< 0.01)	

Applic. Type BCS = broadcast spray

Melons

Table 74 Residues of fluensulfone, BSA, MeS, and TSA in melons following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Montezuma, Georgia, USA 2009 [Ambrosia Hybrid] (09-01859)	4.00	2087	3 days pre-plantin g	drip irrigation	70	< 0.01, < 0.01 (< 0.01)	0.010, < 0.01 (< 0.01)	n.a.	0.067, 0.053 (0.060)
					73	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.045, 0.037 (0.041)
					77	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.010 (< 0.01)	n.a.	0.046, 0.057 (0.052)
					80	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.031, 0.031 (0.031)
Fresno, California, USA 2009 [Yuma Grande F1] (09-01859)	4.00	2083	3 days pre-plantin g	drip irrigation	77	< 0.01, < 0.01 (< 0.01)	0.091, 0.089 (0.090)	n.a.	0.144, 0.177 (0.16)
					80	< 0.01, < 0.01 (< 0.01)	0.117, 0.101 (0.11)	n.a.	0.197, 0.215 (0.21)
					84	< 0.01, < 0.01 (< 0.01)	0.070, 0.074 (0.072)	n.a.	0.146, 0.156 (0.15)
					87	< 0.01, < 0.01 (< 0.01)	0.060, 0.060 (0.060)	n.a.	0.128, 0.128 (0.13)
					91	< 0.01, < 0.01 (< 0.01)	0.050, 0.042 (0.046)	n.a.	0.090, 0.109 (0.10)
King City, California, USA 2010 [Hale's Best	3.93	383	7 d pre-plantin g	BCS	133	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	0.016, 0.018 (0.017)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
Jumbo] (AA100708)									
Arroyo Grande, California, USA 2010 [Top Mark] (AA100708)	3.85	365	7 d pre-plantin g	BCS	97	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Seven Springs, North Carolina, USA 2010 [Hales Best] (AA100708)	4.10	359	7 d pre-plantin g	BCS	66	< 0.01, < 0.01 (< 0.01)	0.061, 0.036 (0.049)	< 0.01, < 0.01 (< 0.01)	0.673, 0.437 (0.56)
Hinton, Oklahoma, USA 2010 [Caravelle] (AA100708)	3.98	253	6 d pre-plantin g	BCS	82	< 0.01, < 0.01 (< 0.01)	**0.065**, 0.062 (0.064)	< 0.01, < 0.01 (< 0.01)	0.303, 0.294 (0.30)
Branchton, Ontario, Canada 2010 [Primo] (AA100708)	4.04	253	6 d pre-plantin g	BCS	80	< 0.01, < 0.01 (< 0.01)	0.015, 0.027 (0.021)	< 0.01, < 0.01 (< 0.01)	0.032, 0.050 (0.041)
Portage la Prairie, Manitoba, Canada 2010 [Athena] (AA100708)	4.11	359	7 d pre-plantin g	BCS	91	< 0.01, < 0.01 (< 0.01)	0.034, 0.030 (0.032)	< 0.01, < 0.01 (< 0.01)	0.172, 0.154 (0.16)
Branchton, Ontario, Canada 2010 [Early sweet] (AA100708)	4.02	251	6 d pre-plantin g	BCS	83	< 0.01, < 0.01 (< 0.01)	0.030, 0.020 (0.025)	< 0.01, < 0.01 (< 0.01)	0.102, 0.091 (0.097)
Corning, California, USA 2010 [ACR 215] (AA100708)	4.02	233	7 d pre-plantin g	BCS	92	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)

Applic. Type BCS = broadcast spray

Residue n.a. = Not analysed

In a magnitude-of-the-residue study by Chevalier (2011, Report R-23486), muskmelon were grown under protected conditions in Southern Europe (Greece, Italy, and Spain) in soil that had been treated with fluensulfone by drip irrigation, at a rate of ca. 4.0 kg ai/ha, 7 days prior to transplanting. The melons were harvested at maturity, 62–79 days after application as well as for residue decline (up to 98 days after application), and stored frozen until preparation for analysis. Preparation consisted of separating the melon samples into their pulp and peel components, homogenizing the fractions, and

then storing them frozen prior to analysis. Analysis was by Method 1977W and the equivalent Method 2061W.

Table 75 Residues of fluensulfone, BSA, MeS, and TSA in melon pulp, peel, and whole fruit following treatment by drip irrigation seven days pre-transplant

Location (Region) Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	DAT, days	Fraction	Residue, mg/kg				Reference
					Fluen.	BSA	MeS	TSA	
cGAP - USA	3.84		–						
La Palma, Murcia, Spain (Southern Europe—Indoor) 2010 [Cantasapo]	3.94	9000	77	peel	< 0.01	0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	0.01	n.a.	< 0.01	
Ramonete, Murcia, Spain (Southern Europe—Indoor) 2010 [Gabriel]	3.94	18000	64	peel	< 0.01	< 0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	< 0.01	n.a.	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	63	peel	< 0.01	< 0.01	< 0.01	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	< 0.01	< 0.01	
				whole fruit	< 0.01	< 0.01	< 0.01	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	66	peel	< 0.01	< 0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	< 0.01	–	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	70	peel	< 0.01	< 0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	< 0.01	–	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	73	peel	< 0.01	0.02	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	0.01	–	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	78	peel	< 0.01	< 0.01	< 0.01	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	< 0.01	< 0.01	
				whole fruit	< 0.01	< 0.01	< 0.01	< 0.01	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Giusto]	3.94	9000	70	peel	< 0.01	0.20	n.a.	0.15	BPL10/237/CL
				pulp	< 0.01	0.09	n.a.	0.04	
				whole fruit	< 0.01	0.13	n.a.	0.08	
Salizzole, Verona, Italy (Southern Europe—Indoor)	3.94	9000	62	peel	< 0.01	0.25	n.a.	0.46	BPL10/237/CL

Location (Region) Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	DAT, days	Fraction	Residue, mg/kg				Reference
					Fluen.	BSA	MeS	TSA	
2010 [Macigno]									
				pulp	< 0.01	0.17	n.a.	0.20	
				whole fruit	< 0.01	0.20	n.a.	0.31	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	67	peel	< 0.01	0.03	< 0.01	0.02	BPL10/237/CL
				pulp	< 0.01	0.02	< 0.01	< 0.01	
				whole fruit	< 0.01	0.02	< 0.01	0.01	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	70	peel	< 0.01	0.04	n.a.	0.04	BPL10/237/CL
				pulp	< 0.01	0.02	n.a.	< 0.01	
				whole fruit	< 0.01	0.03	–	0.02	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	74	peel	< 0.01	0.06	n.a.	0.04	BPL10/237/CL
				pulp	< 0.01	0.02	n.a.	< 0.01	
				whole fruit	< 0.01	0.03	–	0.02	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	77	peel	< 0.01	0.11	n.a.	0.08	BPL10/237/CL
				pulp	< 0.01	0.03	n.a.	0.01	
				whole fruit	< 0.01	0.06	–	0.03	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	81	peel	< 0.01	0.07	< 0.01	0.05	BPL10/237/CL
				pulp	< 0.01	0.01	< 0.01	0.01	
				whole fruit	< 0.01	0.03	< 0.01	0.02	
Chalkidona, Macedonia, Greece (Southern Europe—Indoor) 2010 [Lavigal]	3.94	9000	79	peel	< 0.01	0.01	n.a.	0.07	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	0.02	
				whole fruit	< 0.01	0.01	n.a.	0.05	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	84	peel	< 0.01	0.03	< 0.01	0.15	BPL10/237/CL
				pulp	< 0.01	0.01	< 0.01	0.05	
				whole fruit	< 0.01	0.02	< 0.01	0.10	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	87	peel	< 0.01	0.02	n.a.	0.16	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	0.05	
				whole fruit	< 0.01	0.02	–	0.11	
Nea Magnisia, Macedonia,	3.94	9000	91	peel	< 0.01	0.04	n.a.	0.19	BPL10/237/CL

Location (Region) Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	DAT, days	Fraction	Residue, mg/kg				Reference
					Fluen.	BSA	MeS	TSA	
Greece (Southern Europe—Indoor) 2010 [Galia]									
				pulp	< 0.01	0.02	n.a.	0.09	
				whole fruit	< 0.01	0.03	–	0.14	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	94	peel	< 0.01	0.05	n.a.	0.30	BPL10/237/CL
				pulp	< 0.01	0.01	n.a.	0.09	
				whole fruit	< 0.01	0.03	–	0.19	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	98	peel	< 0.01	0.03	< 0.01	0.14	BPL10/237/CL
				pulp	< 0.01	< 0.01	< 0.01	0.05	
				whole fruit	< 0.01	0.02	< 0.01	0.09	
Average Ratio				peel/fruit	–	1.52	–	1.80	–
				pulp/fruit	–	0.62	–	0.50	–

n.a. = not analysed

Fruiting vegetables, other than Cucurbits

Peppers

Table 76 Residues of fluensulfone, BSA, MeS, and TSA in pepper following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Chili Pepper									
Montezuma, Georgia, USA 2009 [Aristotle X3R] (09-01858)	4.01	2087	3 days pre-plantin g	drip irrigation	53	< 0.01, < 0.01 (< 0.01)	0.019, 0.018 (0.019)	n.a.	0.064, 0.069 (0.067)
					56	< 0.01, < 0.01 (< 0.01)	0.022, 0.020 (0.021)	n.a.	0.073, 0.064 (0.069)
					60	< 0.01, < 0.01 (< 0.01)	0.015, 0.015 (0.015)	n.a.	0.074, 0.069 (0.072)
					63	< 0.01, < 0.01 (< 0.01)	0.016, 0.016 (0.016)	n.a.	0.065, 0.070 (0.068)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
					67	< 0.01, < 0.01 (< 0.01)	0.014, 0.016 (0.015)	n.a.	0.052, 0.058 (0.055)
	4.01	2087	30 days post-plantin g	drip irrigation	20	< 0.01, < 0.01 (< 0.01)	0.230, 0.207 (0.22)	n.a.	0.140, 0.108 (0.12)
					23	< 0.01, < 0.01 (< 0.01)	0.219, 0.202 (0.21)	n.a.	0.125, 0.125 (0.12)
					27	< 0.01, < 0.01 (< 0.01)	0.181, 0.227 (0.20)	n.a.	0.118, 0.147 (0.13)
					30	< 0.01, < 0.01 (< 0.01)	0.184, 0.185 (0.18)	n.a.	0.117, 0.110 (0.11)
					34	< 0.01, < 0.01 (< 0.01)	0.165, 0.206 (0.186)	n.a.	0.090, 0.099 (0.095)
Clermont, Florida, USA 2009 [Patriot] (09-01858)	4.02	2088	3 days pre-plantin g	drip irrigation	65	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					68	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					72	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					75	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					79	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.011, < 0.01 (0.010)
	4.02	2088	36 days post-plantin g	drip irrigation	26	< 0.01, < 0.01 (< 0.01)	0.032, 0.030 (0.031)	n.a.	< 0.01, < 0.01 (< 0.01)
					29	< 0.01, < 0.01 (< 0.01)	0.027, 0.033 (0.030)	n.a.	< 0.01, < 0.01 (< 0.01)
					33	< 0.01, < 0.01 (< 0.01)	0.027, 0.021 (0.024)	n.a.	< 0.01, < 0.01 (< 0.01)
					36	< 0.01, < 0.01 (< 0.01)	0.019, 0.018 (0.019)	n.a.	< 0.01, < 0.01 (< 0.01)
					40	< 0.01, < 0.01 (< 0.01)	0.020, 0.021 (0.021)	n.a.	< 0.01, < 0.01 (< 0.01)
Porterville, California, USA 2010 [Fresno] (AA100707)	3.98	301	7 d pre-plantin g	BCS	83	< 0.01, < 0.01 (< 0.01)	0.049, 0.031 (0.040)	< 0.01, < 0.01 (< 0.01)	0.037, 0.033 (0.035)
	3.93 + 2.0	297 + 9000	7 d pre-plantin g + 40	BCS + drip irrigation	43	< 0.01, < 0.01 (< 0.01)	0.360, 0.392 (0.38)	< 0.01, < 0.01 (< 0.01)	0.137, 0.156 (0.15)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
			d post plant.						
					46	< 0.01, < 0.01 (< 0.01)	0.301, 0.252 (0.28)	< 0.01, < 0.01 (< 0.01)	0.147, 0.139 (0.14)
					51	< 0.01, < 0.01 (< 0.01)	0.282, 0.363 (0.32)	0.011, < 0.01 (0.010)	0.180, 0.155 (0.17)
					53	< 0.01, < 0.01 (< 0.01)	0.265, 0.318 (0.29)	0.010, < 0.01 (< 0.01)	0.118, 0.166 (0.14)
					56	< 0.01, < 0.01 (< 0.01)	0.226, 0.155 (0.19)	< 0.01, < 0.01 (< 0.01)	0.174, 0.145 (0.16)
Oviedo, Florida, USA 2010 [Sweet Banana] (AA100707)	3.90	279	7 d pre-plantin g	BCS	50	< 0.01, < 0.01 (< 0.01)	**0.201**, 0.167 (0.18)	< 0.01, < 0.01 (< 0.01)	0.092, 0.086 (0.089)
	3.92 + 2.0	280 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	3	< 0.01, < 0.01 (< 0.01)	0.250, 0.223 (0.24)	< 0.01, < 0.01 (< 0.01)	0.092, 0.076 (0.084)
Hinton, Oklahoma, USA 2010 [Tam Jalapeno] (AA100707)	4.03	539	7 d pre-plantin g	BCS	101	< 0.01, < 0.01 (< 0.01)	0.044, 0.037 (0.041)	< 0.01, < 0.01 (< 0.01)	0.224, 0.274 (0.25)
	4.08 + 2.0	546 + 9006	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	53	< 0.01, < 0.01 (< 0.01)	0.092, 0.084 (0.088)	0.011, < 0.01 (0.010)	0.389, 0.367 (0.38)
Sweet Pepper									
Fresno, California, USA 2009 [Baron] (09-01858)	4.00	2088	3 days pre-plantin g	drip irrigation	102	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, 0.010 (< 0.01)
					105	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					109	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					112	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					116	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
	4.00	2088	38 days post-plantin g	drip irrigation	61	< 0.01, < 0.01 (< 0.01)	0.041, 0.040 (0.041)	n.a.	0.021, 0.016 (0.019)
					64	< 0.01,	0.025, 0.032	n.a.	0.013, 0.017

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
						< 0.01 (< 0.01)	(0.029)		(0.015)
					68	< 0.01, < 0.01 (< 0.01)	0.029, 0.026 (0.028)	n.a.	0.013, 0.015 (0.014)
					71	< 0.01, < 0.01 (< 0.01)	0.027, 0.021 (0.024)	n.a.	0.015, 0.014 (0.015)
					75	< 0.01, < 0.01 (< 0.01)	0.019, 0.018 (0.019)	n.a.	0.010, 0.011 (0.011)
Porterville, California, USA 2010 [California Wonder] (AA100707)	3.87	342	7 d pre-plantin g	BCS	104	< 0.01, < 0.01 (< 0.01)	0.067, 0.072 (0.070)	< 0.01, < 0.01 (< 0.01)	0.027, 0.027 (0.027)
	4.01	9000	7 d pre-plantin g	drip irrigation	104	< 0.01, < 0.01 (< 0.01)	0.073, 0.062 (0.068)	< 0.01, < 0.01 (< 0.01)	0.080, 0.067 (0.074)
	3.9 + 2.0	345 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	63	< 0.01, < 0.01 (< 0.01)	0.063, 0.055 (0.059)	< 0.01, < 0.01 (< 0.01)	0.031, 0.027 (0.029)
Oviedo, Florida, USA 2010 [Green Bell] (AA100707)	3.97	284	7 d pre-plantin g	BCS	63	< 0.01, < 0.01 (< 0.01)	0.225, **0.239** (0.23)	0.014, 0.012 (0.013)	0.150, 0.188 (0.17)
	3.94 + 2.0	282 + 9108	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	16	< 0.01, < 0.01 (< 0.01)	0.379, 0.372 (0.38)	0.012, 0.010 (0.011)	0.169, 0.170 (0.17)
Seven Springs, North Carolina, USA 2010 [Jupiter] (AA100707)	4.02	351	7 d pre-plantin g	BCS	73	< 0.01, < 0.01 (< 0.01)	0.055, 0.054 (0.055)	< 0.01, < 0.01 (< 0.01)	0.438, 0.483 (0.46)
	3.99 + 2.00	349 + 6279	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	26	< 0.01, < 0.01 (< 0.01)	0.116, 0.141 (0.13)	< 0.01, < 0.01 (< 0.01)	1.056, 1.285 (1.2)
					29	< 0.01, < 0.01 (< 0.01)	0.109, 0.129 (0.12)	< 0.01, < 0.01 (< 0.01)	0.915, 1.030 (0.97)
					33	< 0.01, < 0.01 (< 0.01)	0.166, 0.115 (0.14)	< 0.01, < 0.01 (< 0.01)	1.144, 0.853 (1.0)
					35	< 0.01, < 0.01 (< 0.01)	0.131, 0.052 (0.092)	< 0.01, < 0.01 (< 0.01)	1.012, 0.515 (0.76)
					40	< 0.01, < 0.01 (< 0.01)	0.099, 0.092 (0.096)	< 0.01, < 0.01 (< 0.01)	0.898, 0.933 (0.92)
Hinton, Oklahoma,	4.10	534	7 d pre-plantin	BCS	108	< 0.01, < 0.01	0.086, 0.078 (0.082)	< 0.01, < 0.01	0.341, 0.349 (0.34)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
USA 2010 [XR3 Camelot Sweet Bell] (AA100707)			g			(< 0.01)		(< 0.01)	
	4.11 + 2.00	535 + 9002	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	64	< 0.01, < 0.01 (< 0.01)	0.150, 0.160 (0.16)	< 0.01, < 0.01 (< 0.01)	0.507, 0.424 (0.47)
Thorndale, Ontario, Canada 2010 [Revolution] (AA100707)	3.84	384	7 d pre-plantin g	BCS	63	< 0.01, < 0.01 (< 0.01)	0.065, 0.060 (0.063)	< 0.01, < 0.01 (< 0.01)	0.286, 0.274 (0.28)
	3.85+ 2.00	385 + 900	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	46	< 0.01, < 0.01 (< 0.01)	0.268, 0.244 (0.26)	0.016, 0.017 (0.017)	0.313, 0.348 (0.33)
Portage la Prairie, Manitoba, Canada 2010 [California Wonder] (AA100707)	4.07	355	7 d pre-plantin g	BCS	102	< 0.01, < 0.01 (< 0.01)	0.049, 0.047 (0.048)	< 0.01, < 0.01 (< 0.01)	0.169, 0.162 (0.17)
	4.14+ 2.00	362 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	46	< 0.01, < 0.01 (< 0.01)	0.151, 0.166 (0.16)	< 0.01, < 0.01 (< 0.01)	0.172, 0.162 (0.17)
Branchton, Ontario, Canada 2010 [Aristotle] (AA100707)	3.82	239	7 d pre-plantin g	BCS	76	< 0.01, < 0.01 (< 0.01)	0.027, 0.036 (0.032)	< 0.01, < 0.01 (< 0.01)	0.059, 0.073 (0.066)
	4.00	9000	7 d pre-plantin g	drip irrigation	76	< 0.01, < 0.01 (< 0.01)	0.068, 0.077 (0.073)	< 0.01, < 0.01 (< 0.01)	0.114, 0.118 (0.12)
	4.07 + 4.00	254 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	27	< 0.01, < 0.01 (< 0.01)	0.128, 0.164 (0.15)	< 0.01, < 0.01 (< 0.01)	0.077, 0.075 (0.076)
Portage la Prairie, Manitoba, Canada 2010 [Hungarian Yellow Wax] (AA100707)	4.07	356	7 d pre-plantin g	BCS	102	< 0.01, < 0.01 (< 0.01)	0.141, 0.130 (0.14)	0.012, 0.012 (0.012)	0.198, 0.181 (0.19)
	3.93+ 2.00	344 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	56	< 0.01, < 0.01 (< 0.01)	0.297, 0.275 (0.29)	0.024, 0.019 (0.022)	0.162, 0.143 (0.15)

Applic. Type BCS = broadcast spray

Residue n.a. = not analysed

Tomatoes

Table 77 Residues of fluensulfone, BSA, MeS, and TSA in tomato following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-planting	drip irrig., band applic., broadcast spray	–				
Clermont, Florida, USA 2010 [Celebrity] (09-01858)	4.01	2083	3 days pre-planting	drip irrigation	73	< 0.01, < 0.01 (< 0.01)	0.044, 0.044 (0.044)	n.a.	0.042, 0.037 (0.040)
					77	< 0.01, < 0.01 (< 0.01)	0.021, 0.014 (0.018)	n.a.	0.014, 0.010 (0.012)
					80	< 0.01, < 0.01 (< 0.01)	0.017, 0.014 (0.016)	n.a.	0.016, 0.012 (0.014)
					84	< 0.01, < 0.01 (< 0.01)	0.012, 0.011 (0.012)	n.a.	0.010, 0.010 (0.010)
					87	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					115	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.016, 0.018 (0.017)
Fresno, California, USA 2009 [H 8004 Processing] (09-01858)	4.00	2088	3 days pre-planting	drip irrigation	118	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.024, 0.030 (0.027)
					122	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.023, 0.023 (0.023)
					125	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.026, 0.025 (0.026)
					129	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.022, 0.029 (0.026)
Madera, California, USA 2009 [H 8004 Processing] (09-01858)	3.99	2086	3 days pre-planting	drip irrigation	122	< 0.01, < 0.01 (< 0.01)	0.016, 0.018 (0.017)	n.a.	0.029, 0.023 (0.026)
					125	< 0.01, < 0.01 (< 0.01)	0.012, 0.016 (0.014)	n.a.	0.036, 0.043 (0.040)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
					129	< 0.01, < 0.01 (< 0.01)	0.010, 0.012 (0.011)	n.a.	0.034, 0.024 (0.029)
					132	< 0.01, < 0.01 (< 0.01)	0.018, 0.014 (0.016)	n.a.	0.034, 0.025 (0.030)
					136	< 0.01, < 0.01 (< 0.01)	0.019, 0.014 (0.017)	n.a.	0.028, 0.020 (0.024)
Corning, California, USA 2010 [AB-3] (AA100707)	4.02	233	7 d pre-plantin g	BCS	114	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
	8.02	232	7 d pre-plantin g	BCS	114	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Porterville, California, USA 2010 [Rio Grande] (AA100707)	3.92	296	7 d pre-plantin g	BCS	112	< 0.01, < 0.01 (< 0.01)	0.059, 0.114 (0.087)	< 0.01, < 0.01 (< 0.01)	0.036, 0.053 (0.045)
Porterville, California, USA 2010 [Champion] (AA100707)	3.92	344	7 d pre-plantin g	BCS	146	< 0.01, < 0.01 (< 0.01)	0.014, 0.020 (0.017)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
	4.00	9000	7 d pre-plantin g	drip irrigation	146	< 0.01, < 0.01 (< 0.01)	0.024, 0.033 (0.029)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Livingston, California, USA 2010 [Champion] (AA100707)	3.99	357	7 d pre-plantin g	BCS	126	< 0.01, < 0.01 (< 0.01)	0.035, 0.033 (0.034)	< 0.01, < 0.01 (< 0.01)	0.026, 0.028 (0.027)
King City, California, USA 2010 [Rio Grande] (AA100707)	4.04	395	7 d pre-plantin g	BCS	150	< 0.01, < 0.01 (< 0.01)	0.024, 0.022 (0.023)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Visalia, California, USA 2010 [Champion] (AA100707)	3.94	357	7 d pre-plantin g	BCS	123	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Chico, California, USA 2010 [AB-3] (AA100707)	4.02	232	7 d pre-plantin g	BCS	143	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Arroyo Grande, California, USA 2010	3.64	345	7 d pre-plantin g	BCS	113	< 0.01, < 0.01 (< 0.01)	0.015, 0.010 (0.013)	< 0.01, < 0.01 (< 0.01)	0.018, 0.013 (0.016)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
[Shady Lady] (AA100707)									
Hobe Sound, Florida, USA 2010 [Florida 47] (AA100707)	3.97	228	7 d pre-plantin g	BCS	102	< 0.01, < 0.01 (< 0.01)	0.271, 0.267 (0.27)	< 0.01, < 0.01 (< 0.01)	0.081, 0.100 (0.091)
Dover, Florida, USA 2010 [Tigris] (AA100707)	4.04	215	7 d pre-plantin g	BCS	78	< 0.01, < 0.01 (< 0.01)	**0.275**, 0.270 (0.27)	< 0.01, < 0.01 (< 0.01)	0.086, 0.075 (0.081)
Seven Springs, North Carolina, USA 2010 [Homestead] (AA100707)	4.11	359	7 d pre-plantin g	BCS	94	< 0.01, < 0.01 (< 0.01)	0.027, 0.024 (0.026)	< 0.01, < 0.01 (< 0.01)	0.202, 0.141 (0.17)
North Rose, New York, USA 2010 [Mountain Spring] (AA100707)	4.02	329	7 d pre-plantin g	BCS	93	< 0.01, < 0.01 (< 0.01)	0.058, 0.090 (0.074)	< 0.01, < 0.01 (< 0.01)	0.080, 0.115 (0.098)
Thorndale, Ontario, Canada 2010 [Mariana] (AA100707)	3.81	381	7 d pre-plantin g	BCS	101	< 0.01, < 0.01 (< 0.01)	0.085, 0.102 (0.094)	< 0.01, < 0.01 (< 0.01)	0.222, 0.234 (0.23)
Thorndale, Ontario, Canada 2010 [Heinz 3478] (AA100707)	3.75	375	7 d pre-plantin g	BCS	88	< 0.01, < 0.01 (< 0.01)	0.185, 0.211 (0.20)	< 0.01, < 0.01 (< 0.01)	0.281, 0.247 (0.26)
Portage la Prairie, Manitoba, Canada 2010 [Fantastic] (AA100707)	4.07	356	7 d pre-plantin g	BCS	91	< 0.01, < 0.01 (< 0.01)	0.081, 0.095 (0.088)	< 0.01, < 0.01 (< 0.01)	0.067, 0.088 (0.078)
Elm Creek, Manitoba, Canada 2010 [Fantastic] (AA100707)	4.12	360	7 d pre-plantin g	BCS	79	< 0.01, < 0.01 (< 0.01)	0.260, 0.201 (0.23)	< 0.01, < 0.01 (< 0.01)	0.374, 0.290 (0.33)
Branchton, Ontario, Canada 2010 [TSH 18] (AA100707)	3.98	249	7 d pre-plantin g	BCS	83	< 0.01, < 0.01 (< 0.01)	0.076, 0.067 (0.072)	< 0.01, < 0.01 (< 0.01)	0.128, 0.113 (0.12)
Branchton, Ontario, Canada 2010 [TSH 28] (AA100707)	3.86	241	7 d pre-plantin g	BCS	85	< 0.01, < 0.01 (< 0.01)	0.077, 0.055 (0.066)	< 0.01, < 0.01 (< 0.01)	0.082, 0.067 (0.075)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
	4.00	9000	7 d pre-plantin g	drip irrigation	85	< 0.01, < 0.01 (< 0.01)	0.069, 0.087 (0.078)	< 0.01, < 0.01 (< 0.01)	0.085, 0.106 (0.096)
Branchton, Ontario, Canada 2010 [TSH 25] (AA100707)	4.01	251	7 d pre-plantin g	BCS	83	< 0.01, < 0.01 (< 0.01)	0.180, 0.165 (0.17)	< 0.01, < 0.01 (< 0.01)	0.161, 0.174 (0.17)
Elm Creek, Manitoba, Canada 2010 [Bush Beefsteak] (AA100707)	3.92	296	7 d pre-plantin g	BCS	85	< 0.01, < 0.01 (< 0.01)	0.044, 0.039 (0.042)	< 0.01, < 0.01 (< 0.01)	0.060, 0.050 (0.055)

Applic. Type BCS = broadcast spray

Residue n.a. = not analysed

FATE OF RESIDUES IN STORAGE AND PROCESSING

Nature of the residue during processing

High-temperature hydrolysis

High-temperature hydrolysis of fluensulfone, BSA, MeS, and TSA was investigated by G. Morlock (2011, R-28467). In the study, fluensulfone, BSA, MeS, and TSA were spiked into buffered solutions, in duplicate, at a target concentration of 1 mg/L. The spiked solutions were put into conditions, in the dark, simulating pasteurisation (90 °C, pH 4, 20 min.); baking, brewing, boiling (100 °C, pH 5, 60 min); and sterilisation (120 °C, pH 6, 20 min.). Prior to and after processing, an aliquot from each sample was collected and preserved with acetonitrile. Samples were stored for not more than 17 days, refrigerated (ca. 4 °C) prior to analysis. Analysis consisted of diluting an aliquot of sample with water (fluensulfone, MeS) or acetonitrile/water (BSA, TSA) followed by HPLC-MS/MS determination. Procedural recoveries from samples spiked at 0.1 or 1.0 mg/L ranged from 88 to 102% with standard deviations of not more than 11% across all four compounds and at both spiking levels.

Table 78 Results of high-temperature hydrolysis studies with fluensulfone, BSA, MeS, and TSA (G. Morlock, 2011, R-28467)

	pH		Mass, g		
Analyte	Start	End	Start	End	Recovery
50 mM Citric Acid Buffer, 90 °C, 20 min.					
Fluensulfone	4.03	4.01	224.9	224.9	100.0
	4.03	4.00	225.7	225.7	100.0
TSA	4.02	4.00	224.5	224.4	100.0
	4.02	3.99	223.3	223.1	99.9

MeS	4.02	4.00	224.9	223.9	99.5
	4.02	4.00	225.9	225.9	100.0
BSA	4.02	4.00	226.2	226.2	100.0
	4.02	4.00	225.9	225.8	100.0
50 mM Acetic Acid Buffer, 100 °C, 60 min.					
Fluensulfone	5.04	5.04	221.6	221.5	99.9
	5.04	5.04	225.0	224.8	99.9
TSA	5.05	5.04	224.5	224.2	99.99
	5.04	5.03	224.3	224.2	100.0
MeS	5.05	5.04	224.8	224.8	100.0
	5.05	5.04	223.6	223.6	100.0
BSA	5.05	5.04	223.8	223.6	99.9
	5.05	5.03	226.2	225.9	99.9
50 mM Citric Acid Buffer, 120 °C, 20 min.					
Fluensulfone	6.02	6.01	226.4	226.1	99.9
	6.01	6.01	224.8	224.4	99.8
TSA	6.01	6.01	222.5	222.3	99.9
	6.01	6.01	224.9	224.6	99.9
MeS	6.02	6.01	226.4	226.0	99.8
	6.01	6.01	226.4	226.0	99.8
BSA	6.02	6.02	225.8	225.5	99.9
	6.02	6.01	225.1	225.2	100.0

Residues after processing

The fate of fluensulfone and its BSA, MeS, and TSA metabolites during processing of raw tomato into processed tomato products was investigated by Jones (2011, Report AA100707) by Burn and Winner (2012, Report FOZ1001), and by Jones (2013, Report R-29577). In all studies, samples of processed commodities were generated using procedures reflective of commercial practices and all samples were analysed by methods equivalent to Method 1977W or Method 2061W.

In Jones 2011, tomatoes were transplanted into plots that had received treatment with fluensulfone seven days prior to transplanting at a rate of 7.93 or 8.02 kg ai/ha. Tomatoes were harvested at maturity from the second trial only (8.02 kg ai/ha) and processed into juice, puree, and paste using simulated commercial practices. RAC and processed commodities were assayed for fluensulfone, BSA, MeS, and TSA. All residues were < 0.01 mg/kg in all samples except for parent fluensulfone at 0.01 mg/kg in tomato juice. Given the results and that other studies are available, further information on processing practices and derivation of processing factors are not addressed in this evaluation.

In Burn and Winner, tomatoes were transplanted in to plots which had received fluensulfone seven days prior to transplanting at a rate of either 3.93 or 7.86 kg ai/ha. Tomatoes were harvested at maturity and processed into peeled, canned, sundried, juice, puree, paste, wet pomace, and dry pomace processed commodities using simulated commercial practices. Raw tomato and processed tomato samples were analysed by a method equivalent to Method 2061W.

Peeled tomatoes were made steaming tomatoes, with stems removed, in a steamer pot for six minutes. After steaming, the skins were removed manually and the tomato cores were removed with a standard kitchen coring tool.

Canned tomatoes were made by placing portions of the peeled tomatoes into containers, topping the containers off with juice from the whole tomato, fitting lids to the containers, and boiling in a water-filled pot for 45 minutes. The canned tomatoes were then cooled rapidly to prevent overcooking.

Juice, puree, paste, and wet pomace were made as follows: Whole tomato samples were chopped in a food processor at low speed. The resulting homogenate was strained using a press and a gauze bag to remove course components (skins, seeds, etc.). The material in the bag made up the wet pomace fraction and the strained liquid made up the juice fraction. An aliquot of juice was concentrated, by rotary evaporation in vacuo at 90 °C, to a moisture content of 86% to form puree, and a separate aliquot of juice was concentrated in the same fashion to a moisture content of 72% to form paste. Dry pomace was made by drying wet pomace in an oven to a moisture content of < 10%.

For sundried tomatoes, whole tomato samples were quartered lengthwise and composited into samples containing at least 1 quarter from 12 different tomatoes. The wedges were laid out onto a tray and lightly covered with salt (NaCl, ca. 10–15 g per kg fresh sample). The samples were dried in the sun over a 5-day period. Samples were checked daily for water content and were considered to be suitably dried when they had dehydrated to < 20% of their original weight.

Residues of fluensulfone were < 0.01 mg/kg in all samples. Quantifiable residues of BSA, MeS, and TSA occurred in RAC tomatoes from at least one of the treatment rates. Residues of BSA and TSA were concentrated, relative to the residues in the RAC, in wet and dry pomace. In addition, BSA showed concentration in sundried tomato. MeS was concentrated in dry pomace from the lower treatment rate only.

Table 79 Residues of fluensulfone, BSA, MeS, and TSA in tomato and processed commodities (Burn and Winner, 2012, Report FOZ1001)

	Residue, mg/kg		Processing Factor	
Tomato Commodity	3.93 kg ai/ha rate	7.86 kg ai/ha rate	3.93 kg ai/ha rate	7.86 kg ai/ha rate
Fluensulfone				
Raw fruit	< 0.01	< 0.01	–	–
Canned	< 0.01	< 0.01	–	–
Dry pomace	< 0.01	< 0.01	–	–
Peeled	< 0.01	< 0.01	–	–
Sundried	< 0.01	< 0.01	–	–
Juice	< 0.01	< 0.01	–	–
Paste	< 0.01	< 0.01	–	–
Puree	< 0.01	< 0.01	–	–
Wet pomace	< 0.01	< 0.01	–	–
BSA				
Raw fruit	0.01	0.03	–	–
Canned	< 0.01	0.01	< 1	0.33
Dry pomace	0.17	0.28	17	9.3
Peeled	< 0.01	0.01	< 1	0.33
Sundried	0.02	0.05	2	1.67
Juice	< 0.01	0.02	< 1	0.67
Paste	0.01	0.03	1	1
Puree	< 0.01	0.02	< 1	0.67
Wet pomace	0.04	0.09	4	3

	Residue, mg/kg		Processing Factor	
Tomato Commodity	3.93 kg ai/ha rate	7.86 kg ai/ha rate	3.93 kg ai/ha rate	7.86 kg ai/ha rate
MeS				
Raw fruit	0.02	< 0.01	–	–
Canned	< 0.01	< 0.01	< 0.5	–
Dry pomace	0.04	0.05	2	–
Peeled	< 0.01	< 0.01	< 0.5	–
Sundried	< 0.01	0.01	< 0.5	–
Juice	< 0.01	< 0.01	< 0.5	–
Paste	< 0.01	< 0.01	< 0.5	–
Puree	< 0.01	< 0.01	< 0.5	–
Wet pomace	< 0.01	0.02	< 0.5	–
TSA				
Raw fruit	0.01	0.02	–	–
Canned	< 0.01	< 0.01	< 1	< 0.5
Dry pomace	0.06	0.09	6.0	4.5
Peeled	< 0.01	0.01	< 1	0.5
Sundried	0.01	0.02	1	1
Juice	< 0.01	< 0.01	< 1	< 0.5
Paste	0.01	0.01	1	0.5
Puree	< 0.01	< 0.01	< 1	< 0.5
Wet pomace	0.02	0.03	2	1.5

In a second study by Jones (2013, R-29577), tomatoes were planted into plots treated at a rate of either 12 kg ai/ha or 20 kg ai/ha seven days prior to transplanting. Tomatoes were harvested from one plot at the higher treatment rate and processed into juice, puree, paste, and wet and dry pomace using simulated commercial practices. Residues of fluensulfone, BSA, MeS, and TSA were assayed using Method 2061W.

Prior to processing, tomatoes were washed (52–57 °C, 3–5 min), hand culled, and suitable fruits were trimmed of defects and/or off-colour areas. Cleaned tomatoes were chopped to a fine consistency and processed through a pulper/finisher with a 2.4 mm screen. Material passing through the screen underwent a hot-break process and was then passed through a pulper/finisher fitted with a 0.84 mm screen. An aliquot of the material passing through the screen was heated (85–91 °C, 3 min), placed into cans, pressure cooked (121–124 °C, 40–45 seconds), and cooled in a water bath (16–27 °C, 28–32 min). The resulting juice fraction was then placed into frozen storage. Separate aliquots of the juice fraction were vacuum-evaporated to form puree (8–24% solids) and paste (24–30% solids). Puree and paste samples were heated, canned, and cooled, as above for juice (no pressure cooking). Material not passing through the screens was collected as wet pomace, of which an aliquot was dried (54–71 °C, 20–24 hrs) to form dry pomace.

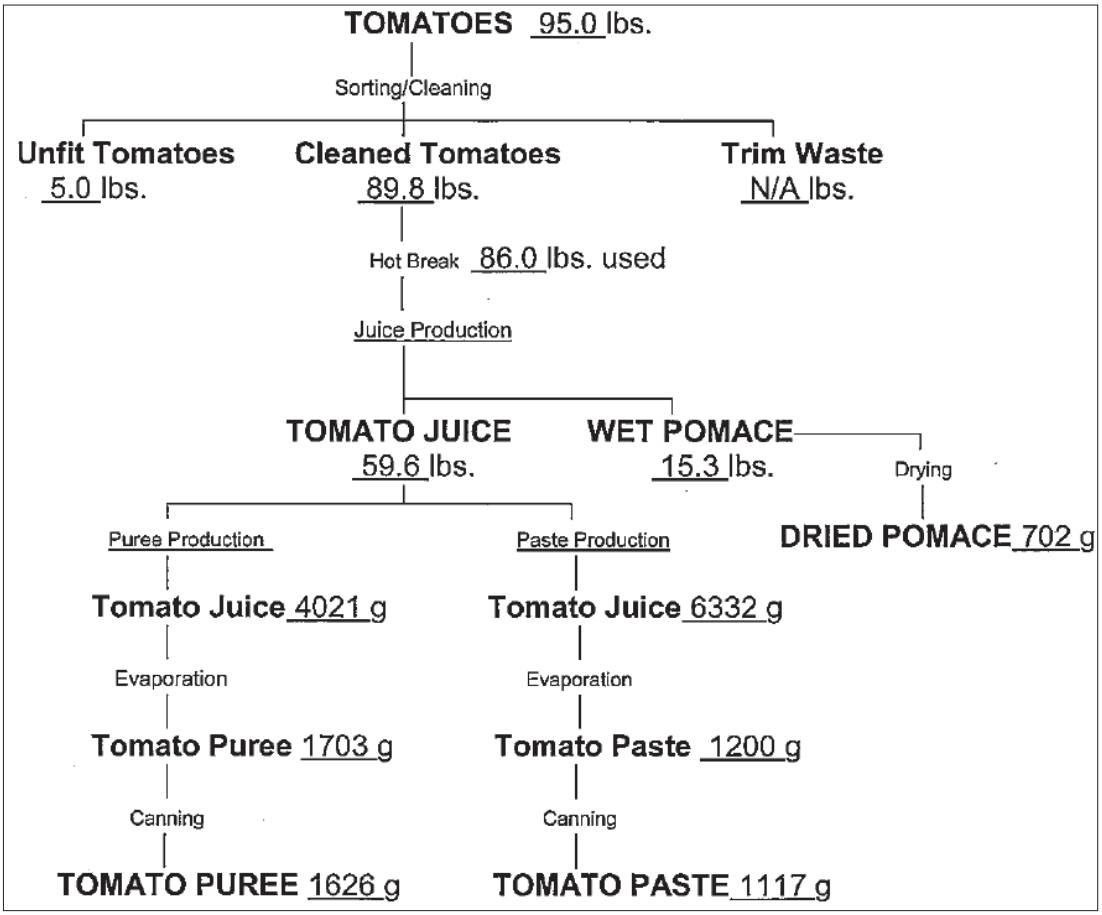


Figure 6 Material balance and processed commodity flowchart for processed tomato commodities (copied without alteration from Jones 2013, Report R-29577)

Residues of fluensulfone and MeS were < 0.01 ppm in all commodities. Residues of BSA and TSA were quantifiable in all commodities and showed concentration, relative to the raw fruit, in dry pomace and paste, and a slight concentration in BSA in puree.

Table 80 Residues of fluensulfone, BSA, MeS, and TSA in tomato and processed commodities (Jones, 2013, Report R-29577)

Tomato Commodity	Average residue, mg/kg	Processing factor
Fluensulfone		
Raw fruit	< 0.01	–
Dry pomace	< 0.01	–
Juice	< 0.01	–
Paste	< 0.01	–
Puree	< 0.01	–
Wet pomace	< 0.01	–
BSA		
Raw fruit	2.17	–
Dry pomace	14.26	6.57
Juice	1.81	0.83
Paste	7.69	3.54
Puree	3.00	1.38

Tomato Commodity	Average residue, mg/kg	Processing factor
Wet pomace	1.43	0.66
MeS		
Raw fruit	< 0.01	–
Dry pomace	< 0.01	–
Juice	< 0.01	–
Paste	< 0.01	–
Puree	< 0.01	–
Wet pomace	< 0.01	–
TSA		
Raw fruit	0.50	–
Dry pomace	1.73	3.46
Juice	0.46	0.92
Paste	1.41	2.82
Puree	0.49	0.98
Wet pomace	0.36	0.72

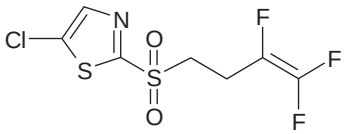
Residues in animal commodities

No feeding studies depicting transfer of residues from animal feeds to animal commodities were provided.

APPRAISAL

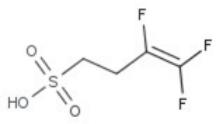
Fluensulfone is a non-fumigant nematicide in the fluoroalkenyl class of pesticides. Fluensulfone shows activity in multiple nematicide physiological systems. It was considered for the first time by the 2013 JMPR for toxicology and by the 2014 JMPR for residues. The 2013 JMPR established an ADI of 0–0.01 mg/kg bw and an ARfD of 0.3 mg/kg bw.

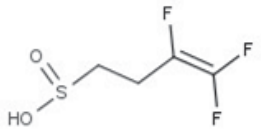
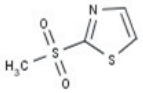
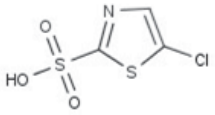
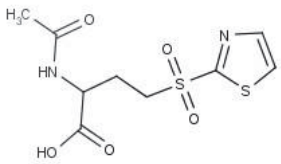
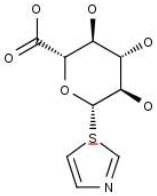
The IUPAC name for fluensulfone is 5-chloro-1,3-thiazol-2-yl 3,4,4-trifluorobut-3-en-1-yl sulfone.



Fluensulfone with ^{14}C radiolabelling in the thiazole ring or in the ethane bridge between the sulfone and trifluorobutene moieties was used in the metabolism and environmental fate studies. In this appraisal, these positions are referred to as the Th and Bu labels, respectively.

The following abbreviations, along with IUPAC names and structures, are used for the metabolites discussed in this appraisal:

BSA	3,4,4-trifluorobut-3-ene-1-sulfonic acid	

Butene sulfinic acid	3,4,4-trifluorobut-3-ene-1-sulfinic acid	
MeS	2-methylsulfonyl-1,3-thiazole	
TSA	5-chloro-1,3-thiazole-2-sulfonic acid	
Thiazole mercapturate	2-acetamido-4-(1,3-thiazole-2-sulfonyl)butanoic acid	
Thiazole glucuronides (α and ß isomers)	Name not specified	

Animal metabolism

The Meeting received studies elucidating the metabolism of fluensulfone in laboratory animals (evaluated by the 2013 Meeting), lactating goats, and laying hens.

In rats, absorption of fluensulfone administered by gavage at 5 mg/kg bw is rapid, with maximal plasma concentrations achieved within 4 hours. At 5 and 500 mg/kg bw, the extent of oral absorption is high (> 80%). Fluensulfone is widely distributed in the body. High concentrations of both butene- and thiazole-labelled material were found in the liver and kidney. The labelled material was rapidly excreted via urine (> 70%), with faecal excretion accounting for no more than 5–13%. Absorbed fluensulfone was extensively metabolized, with almost no unmetabolized parent compound detected. Other than low amounts of thiazole sulfonic acid, no other faecal metabolites were present at levels above 5% of the administered dose. The parent compound probably reacts with glutathione and cleaves, giving rise to thiazole mercapturate, thiazole glucuronide, and butene sulfinic acid, the major urinary metabolites.

In goats dosed for five consecutive days at approximately 28.8 mg/animal/day (10.5 ppm in the diet), most of the recovered radioactivity was in urine and GI tract/faeces, with only 10.7% (Th-14C) or 3.5% (Bu-14C) of the applied dose (AD) accounted for in tissues and body fluids. In excreta, the major identified residues were trifluorobutene sulfinic acid and the MeS metabolite. In other matrices, the highest levels of radioactivity were associated with liver (max. 2.6 mg eq./kg, 1.7% AD), kidney (max 1.4 mg eq./kg, 0.2% AD), and milk fat (2.0 mg eq./kg, 0.31% AD). Seventy-five to

ninety percent of the radioactivity in the goat matrices was extracted with a combination of solvent extraction and alkaline digestion. No BSA, TSA, or fluensulfone was detected in any goat matrix. Radioactivity in milk and tissues was primarily associated with glucose (0.039–0.24 mg/kg; 4–17% TRR), lactose (0.036–0.21 mg/kg; 4–63% TRR), proteins/amino acids (0.015–1.2 mg/kg; 5–37% TRR), and triglycerides/fatty acids (0.009–1.1 mg/kg; 7.6–52% TRR), and the radioactivity appears to be due to incorporation of the radiolabelled carbon.

In hens dosed for seven consecutive days at 1.25 mg/animal/day (9.8 ppm in the diet), total radioactive residues (TRR) in excreta accounted for approximately 80% of the dosed material for both label positions. Total radioactivity in eggs did not plateau within the eight dosing days of the hen study. Radioactive residues in eggs were not identified. Most residues in eggs were associated with aqueous phases in the extraction schemes; however, 0.18 mg eq./kg from the butane label (27% TRR) was extracted with hexane:acetone. Fluensulfone was a major residue (0.009–0.041 mg/kg; 21–55% TRR) in poultry fat; otherwise, parent fluensulfone was not observed in any matrix. Comparison of extraction of radioactivity from liver samples treated with and without protease enzyme indicates that ca. 0.16 mg/kg (24%) of the radioactivity was associated with proteins and/or amino acids and approximately 3% (0.016 mg/kg) was identified as TSA. Incorporation of the radioactivity into triglycerides was noted in both fat matrices and in eggs. In eggs, triglyceride accounted for 7% and 27% of the TRR for the thiazole and butene labels, respectively. In fat matrices, triglycerides accounted for 7–12% and 79–87% of the TRR for the thiazole and butene labels, respectively.

Overall, the animal metabolism studies show that fluensulfone is well absorbed and that the majority (75–90%) of the dosed radioactivity is excreted. Results from rat, goat, and hen studies indicate that fluensulfone is cleaved at the sulfonyl bridge in all three animals; however, the identification of different residues in the studies suggests that there may be different metabolic pathways. In both poultry and goats, fluensulfone can be expected to break down and be incorporated almost entirely into natural products. Based on the residue profile in poultry and the observed incorporation of radioactivity into natural components, the Meeting is of the opinion that the lack of a residue plateau in egg is not of concern.

Plant metabolism

The Meeting received studies depicting the metabolism of fluensulfone in tomato, lettuce, and potato. All of the studies were conducted with fluensulfone which was radiolabelled, separately, in the thiazole ring and the ethane bridge between the sulfonyl and trifluorobutene moieties.

To investigate the metabolism of fluensulfone on tomato, fluensulfone was applied at a rate of 4.07 kg ai/ha to soil. Later that same day, tomato seedlings were planted. Mature fruits were harvested 87 days after treatment. Total radioactive residues in tomato were higher in samples treated with Bu-^{14}C-labelled material (0.52 mg eq./kg) than those from Th-^{14}C treatment (0.27 mg eq./kg). The majority (88.7% Th-^{14}C; 91.3% Bu-^{14}C) of the radioactivity was extracted with acetonitrile:water

(ACN:H_2O). TSA made up 0.12 mg/kg (45.4% TRR), with an additional 0.06 mg eq./kg (21.2% TRR) as salts/related compounds. BSA occurred at 0.22 mg/kg (41.6% TRR) with salts/related compounds making up 0.13 mg eq./kg (26.5% TRR). No other compounds, including parent fluensulfone, were identified in tomato.

Lettuce seeds were planted into soil and then fluensulfone was applied at a rate of 4.07 kg ai/ha. Samples were collected 49 days and 64 days after application to obtain immature and mature lettuce, respectively. Contrary to the results with tomato, TRR were higher from treatment with Th-^{14}C-labelled material (6.1–7.1 mg eq./kg) than with Bu-^{14}C-labelled material (1.5–2.4 mg eq./kg) and were similar in immature and mature foliage. The majority of the radioactivity was extracted with ACN:H_2O, with higher extraction efficiency from samples treated with the Th-^{14}C label. Following treatment with Th-^{14}C-labelled material, 3.57 mg/kg and 4.34 mg/kg (67.5% and 70.6% TRR) was identified as TSA in immature and mature leaves, respectively. An additional 1.39 mg eq./kg and 0.41 mg eq./kg (17.8% and 6.6% TRR) in immature and mature leaves, respectively, was determined to be salts and/or other forms of TSA. Following treatment with Bu-^{14}C-labelled material, BSA occurred at 0.49 mg/kg (23.8% TRR) in immature leaves and at 0.49 mg/kg (37.6% TRR) in mature leaves. As with TSA, salts and other forms occurred for BSA and constituted, in total, 0.75 mg eq./kg (36.0% TRR) in immature foliage and 0.29 mg eq./kg (22.1% TRR) in mature foliage. Fluensulfone occurred at trace levels (0.009 mg/kg, 0.008 mg/kg) in immature lettuce from the Th-^{14}C and Bu-^{14}C treatments, respectively. Aside from BSA and TSA, no other metabolites of fluensulfone were identified.

Potato seed pieces were planted just prior to application of fluensulfone to soil at a rate of 4.04 kg ai/ha (Th-^{14}C) or 4.13 kg ai/ha (Bu-^{14}C). Immature (70 days after treatment) and mature (106 days after treatment) tubers were harvested and analysed. For immature and mature tubers, respectively, TRR were 0.32 and 0.44 mg eq./kg from the Th-^{14}C treatment and 0.22 and 0.17 mg eq./kg from the Bu-^{14}C treatment. Extraction with ACN:H_2O efficiently released residues: 91.9% TRR (Th-^{14}C, immature tuber), 91.7% TRR (Th-^{14}C, mature tuber), 76.9% TRR (Bu-^{14}C, immature tuber), and 79.1% TRR (Bu-^{14}C, mature tuber). Fluensulfone was found at trace levels (0.005 mg/kg) from both label treatments in mature tubers only. Otherwise, the only identified residues were BSA, TSA, and their salts and/or related compounds. BSA constituted 0.069 mg/kg (30.7% TRR) and 0.042 mg/kg (25.8% TRR) in immature and mature tubers, respectively. Salts and related forms of BSA provided an additional 0.041 mg eq./kg (17.8% TRR; immature tubers) and 0.035 mg eq./kg (21.4% TRR; mature tubers). TSA occurred at 0.21 mg/kg (63.0% TRR) and 0.31 mg/kg (65.3% TRR) in immature and mature tubers, respectively. Salts and related forms of TSA gave an additional 0.028 mg eq./kg (8.4% TRR; immature tubers) and 0.025 mg eq./kg (5.3% TRR; mature tubers).

Fluensulfone was extensively metabolised in all of the studies, with the only major residues being the BSA and TSA metabolites. A few chromatographic fractions contained radioactivity in

excess of 10% TRR. Investigation of these fractions indicated that the residues were associated with the BSA or TSA metabolites, as salts of the sulfonic acids or as related forms of the metabolites. The only major residues in the harvested matrices were the BSA and TSA metabolites and, with the exception of trace levels of fluensulfone in immature lettuce and mature potato, no parent compound was detected.

Environmental fate in soil

Fluensulfone is stable to hydrolysis under accelerated conditions (50 °C, pH 4, 7, 9) but is prone to photolysis [DT_{50} of 21days (Th-^{14}C) or 35 days (Bu-^{14}C) in soil], showing first-order kinetics. In an aerobic soil metabolism study, major residues following treatment with fluensulfone were BSA, TSA, and MeS, depending on the duration of incubation. Fluensulfone had DT_{50} estimates ranging from 7 to 17 days across six soils, all following first-order kinetics. BSA formed from fluensulfone generally accumulated for the first ca. 1 month of incubation followed by dissipation (DT_{50} 18–26 days). Residues of TSA accumulated continuously over the incubation period, reaching maxima of 49–74% of the applied radioactivity at the 120-day sampling. Residues of MeS began to be observed after the first 2–4 weeks of incubation, reaching a maximum of not more than 8% of the applied radioactivity; residues of MeS declined to 0% of the applied radioactivity between the 50- and 120-day sampling times, depending on the soil. In a separate study, the DT_{50} estimates for the TSA and MeS metabolites under aerobic soil conditions are 421 and 33 days, respectively. Field dissipation studies were not provided.

Confined rotational crop studies were conducted with radish, lettuce, and wheat at plant-back intervals (PBIs) of 30, 120, and 360 or 390 days. Fluensulfone, radiolabelled as either the Th-^{14}C or Bu-^{14}C, was applied to soil at a rate of approximately 4 kg ai/ha. Lettuce was replanted at 390 days after application due to crop failure at the 360-day PBI. Following treatment with Th-^{14}C-labeled material, TRR generally declined sharply from 30 to 120 days and then remained relatively consistent between the 120 and the 360/390-day PBIs. (e.g., wheat hay: 27 mg eq./kg at 30-Day PBI, 9.4 mg eq./kg at 120-Day PBI, 10.8 mg eq./kg at 360-Day PBI) As with primary crops, the major residues were the BSA and TSA metabolites. A low level of the parent compound was observed in lettuce, radish root, radish foliage, and wheat forage, hay, and straw (but not grain). Fluensulfone, when found, was typically 1 to 2 orders of magnitude less than the BSA or TSA residue levels. In all cases, residues of fluensulfone and BSA were not quantifiable after the 120-day PBI whereas residues of TSA persisted at quantifiable levels for at least one year, ranging from 0.13 mg eq./kg (immature lettuce) to 11 mg eq./kg (wheat hay).

Overall, fluensulfone can be expected to dissipate rather rapidly in the environment, with a concomitant increase in residues of BSA, TSA, and, to a much lesser extent, MeS. BSA residues should then decline; however, TSA appears to be stable for an extended period. The Meeting concluded from the soil metabolism and confined rotational crop studies that TSA may accumulate in

soils following repeated uses of fluensulfone and may occur in follow-on crops at plant-back intervals exceeding one year after treatment.

Methods of residue analysis

The Meeting received analytical methods for the analysis of fluensulfone, BSA, MeS, and TSA in plant and animal matrices. The methods are essentially identical for all samples and the LOQ for all matrices and analytes, defined as the lower limit of method validation, is 0.01 mg/kg.

Extraction of residues is accomplished with ACN:H_2O (1:1, v/v) or ACN (BSA and TSA in eggs only); the extract is then split for analysis of fluensulfone and MeS by one set of procedures and for analysis of BSA and TSA by a second set. For fluensulfone and MeS, there is no clean-up of the extract beyond filtration (except hexane partitioning for analysis of MeS in fatty/oily samples). Residues of fluensulfone and MeS are determined by reverse-phase LC-MS/MS in positive ion spray mode. For BSA and TSA, an aliquot of the initial extract is concentrated and then cleaned-up using C-18 SPE. Residues are determined by reverse-phase LC-MS/MS in negative ion spray mode.

The solvent used for extraction is the same as, or very similar to, that used in the metabolism studies and showed adequate extraction efficiency of incurred residues.

Testing of fluensulfone and the two sulfonic acid metabolites, BSA and TSA, through the FDA PAM multiresidue method protocols demonstrated that the compounds showed poor sensitivity, poor recovery, and/or poor chromatography. Overall, the results indicate that the FDA PAM multiresidue protocols are not suitable for the detection or enforcement of fluensulfone, BSA, or TSA residues in non-fatty foods.

Stability of residues in stored analytical samples

The Meeting received data depicting the stability of residues of fluensulfone, BSA, and TSA in tomato, pepper, cucumber, and melon. In addition, the stability of those analytes and MeS was investigated in frozen, stored tomato puree and paste. No dissipation of any analyte was observed during the storage periods for the various matrices. Stability was demonstrated in tomato raw agricultural commodity (RAC) for at least 469 days (ca. 15 months) and in tomato processed commodities for at least 181 days (ca. 6 months). For pepper, cucumber, and melon, residues were stable for at least 488 days (ca. 16 months).

Definition of the residue

Studies depicting the nature of the residues in animals consistently show fluensulfone to be cleaved at the sulfonyl moiety, presumably via glutathione conjugation, resulting in both halves of the molecule having a sulfonyl functional group. With the exception of poultry fat, fluensulfone was not observed in any animal commodity. In livestock, the majority of the radiolabel was excreted. Retained fluensulfone is extensively metabolized, with the radioactivity being associated primarily with sugars,

amino acids, and fatty acids. MeS and butene sulfinic acid were identified in livestock studies, but were observed only in excreta. In the rats, significant residues were thiazole mercapturate, thiazole glucuronide, BSA, TSA, and butene sulfinic acid. MeS, observed in some field trial samples, was not identified in the rat metabolism study.

Based on the livestock metabolism studies, a residue definition potentially suitable for enforcement by the typical criteria is possible only for poultry fat and poultry liver, which were the only matrices in the animal metabolism studies with quantifiable residues of a fluensulfone-specific compound (fluensulfone in fat and TSA in liver). Although fluensulfone was a major residue in poultry fat (up to 55% TRR), the available residue data indicate that quantifiable residues of the parent compound are not expected in plants; thus exposure to fluensulfone via livestock diets is unlikely, making the parent compound an unsuitable marker for enforcement in any livestock commodity. The other potential marker, TSA, occurred only as a minor component in poultry liver (2.7% TRR). Based on the results of the metabolism studies and on the residue profiles observed in crop metabolism studies, confined rotational crop studies, and supervised residue trials, the Meeting determined that a residue definition for livestock commodities is not necessary.

In both plant and rotational crop metabolism studies, fluensulfone appears to follow the same glutathione-mediated pathway observed in livestock; however, in plants quantifiable residues of the BSA and TSA metabolites were consistently observed. Parent fluensulfone was identified only at trace levels in immature lettuce, mature potato, and rotational lettuce, radish foliage, and wheat hay, forage and straw at short PBIs (30 days). In target crops, BSA ranged from 0.071–1.24 mg/kg (43.6–68.1% TRR) and TSA ranged from 0.17–4.75 mg/kg (66.6–85.3% TRR). In rotational crops, BSA was detected in all matrices except wheat grain at the 30-day PBI (0.004–1.4 mg/kg) and in most matrices at the 120-day PBI (0.001–0.43 mg/kg), and was undetected (< 0.001 mg/kg) by the 360/390-day PBI, except wheat straw at 0.012 mg/kg. In contrast, TSA was detected in all rotational crop matrices at all PBIs, ranging from 0.086 mg/kg to 16 mg/kg across all samples.

In crop field trials, fluensulfone was detected in only one sample (summer squash at 0.017 mg/kg). Across all crops, residues of BSA ranged from < 0.01 to 0.27 mg/kg and TSA ranged from < 0.01 to 0.71 mg/kg. MeS ranged from < 0.01 to 0.08 mg/kg and was less than both BSA and TSA in the corresponding sample. In all trials with only pre-plant applications (per GAP), MeS was < 0.01 mg/kg in all samples of cantaloupe, pepper, and tomato. Although MeS was not found in the plant or rotational crop metabolism studies, it was observed in supervised residue trials in cucumber (< 0.01–0.079 mg/kg) and summer squash (< 0.01–0.050 mg/kg).

The Meeting determined that fluensulfone is NOT a suitable marker for compliance with MRLs in crops. Both BSA and TSA are suitable markers based on results of supervised field trials. The confined rotational crop study, however, demonstrates a potential for TSA to carry over into succeeding crops. Therefore, given that quantifiable residues of fluensulfone are not expected in plant commodities, that a separate analysis is required for the analysis of fluensulfone and BSA/TSA, and

that residues of TSA may occur from previous crop cycle treatments with fluensulfone, the Meeting determined that BSA is the most suitable marker for MRL compliance. A validated method exists for analysis of BSA in plant commodities. The Meeting defined the BSA metabolite as the residue definition for compliance in plants.

Regarding the toxicity of the BSA, TSA, and MeS metabolites, the JMPR has concluded that TSA is unlikely to be of any toxicological relevance; data are insufficient at this time to make a definitive toxicological determination regarding the relevancy of BSA and MeS.

For BSA, the JMPR has determined that the ADI and ARfD for fluensulfone could be used as a screening evaluation of exposure to BSA. Based on a comparison of toxicity data between BSA and fluensulfone, the evaluation may be made directly, without a correction for molecular weight. If additional uses are considered in the future, the use of the fluensulfone points of departure to evaluate exposure to BSA may need to be re-evaluated.

For MeS, the JMPR has determined that the IEDI (0.07 µg/kg bw/day) for MeS should be compared to the Cramer class III TTC value of 1.5 µg/kg bw/day and that the IESTI (3.2 µg/kg bw/day)[2] should be compared to the single-exposure TTC for Cramer class III compounds of 5 µg/kg bw proposed by EFSA. The IESTI is somewhat refined in that for melon, the specific HR (0.01 mg/kg) from melon field trials was used rather than the HR for the fruiting vegetables, Cucurbits group (0.053 mg/kg). On the basis of these comparisons, the Meeting concluded that MeS is not considered to be a relevant metabolite for the crops under consideration. If additional uses are considered in the future, this conclusion may need to be re-evaluated.

Given the residue profile in crops and taking into consideration the available information on the toxicities of the metabolites, the Meeting determined that the residue definition for dietary exposure from crops is BSA. In lieu of BSA-specific toxicological points of departure, dietary intake estimates for BSA should be compared to the ADI and ARfD for fluensulfone, with no correction for molecular weight.

Definition of the residue for compliance with the MRLs and dietary intake for plant commodities: *BSA {3,4,4-trifluorobut-3-ene-1-sulfonic acid}*.

Definition of the residue for compliance with the MRLs and for dietary intake for animal commodities: *Not necessary*

Results of supervised residue trials on crops

Fluensulfone is registered in the USA for use on cucurbit vegetables and on fruiting vegetables. For all crops, the cGAP is an application to the soil at 2.8 kg ai/ha made seven days prior to transplanting

[2] The estimate of 3.2 µg/kg bw is refined, using the observed HR for melon (0.01 mg/kg) rather than the HR for the fruiting vegetables, Cucurbits group (0.053 mg/kg), which resulted in a maximum dietary intake estimate of 5.3 µg/kg bw.

crops into the field. Application may be made by broadcast spray to the soil, by banded spray, or by drip irrigation. The applied material must be mechanically incorporated 15–20 cm into the soil profile for spray applications or by sufficient volume for drip irrigation application.

The Meeting received supervised residue trial data for cucumber, summer squash, cantaloupe, pepper, and tomato. The trials were conducted in North America (USA and Canada). All trials were conducted at a target application rate of 3.9 kg ai/ha, which reflects a nominal exaggeration of 39% relative to the cGAP. Therefore, the Meeting decided to scale residue values for all analytes from trials otherwise meeting the cGAP to an application rate of 2.8 kg ai/ha. Residues scaled to < 0.01 mg/kg were maintained at < 0.01 mg/kg. Reported values are field trial averages unless otherwise noted.

Residues of fluensulfone were < 0.01 mg/kg in all samples.

Fruiting vegetables, Cucurbits

In cucumber, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 7) were: < 0.01, 0.01 (2), 0.063, 0.07, 0.17, and 0.219 mg/kg.

Application rates for these trials ranged from 3.72 kg ai/ha to 4.11 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01 (3), 0.041, 0.045, 0.114, and 0.137 mg/kg.

In summer squash, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 8) were: < 0.01, 0.05, 0.06, 0.082, 0.186, 0.196, 0.214, and 0.247 mg/kg.

Application rates for these trials ranged from 3.80 kg ai/ha to 4.14 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01, 0.032, 0.038, 0.051, 0.115, 0.12, 0.133, and 0.149 mg/kg.

In melon, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 8) were: < 0.01 (3), 0.021, 0.025, 0.032, 0.049, and 0.064 mg/kg.

Application rates for these trials ranged from 3.85 kg ai/ha to 4.11 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01 (3), 0.013, 0.016, 0.019, 0.030, and 0.040 mg/kg.

Noting that the GAP in the USA is for the cucurbit vegetables crop group, which is equivalent to the Codex fruiting vegetables, Cucurbit group, and that the BSA residue data from cucumbers, summer squash, and melons are not significantly different by the Kruskal-Wallis test, the Meeting determined that the residues from the trials are similar and is estimating a group maximum residue level for fruiting vegetables, Cucurbits based on the following scaled BSA residue data set (n = 23): < 0.01 (7), 0.013, 0.016, 0.019, 0.030, 0.032, 0.038, 0.040, 0.041, 0.045, 0.051, 0.114, 0.115, 0.120, 0.133, 0.137, and 0.149 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg for BSA on fruiting vegetables, Cucurbits; the HR is 0.16 mg/kg (from a single sample) and the STMR is 0.032 mg/kg.

Fruiting vegetables, other than Cucurbits

In chilli pepper, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 3) were: 0.040, 0.041, and 0.184 mg/kg.

Application rates for these trials ranged from 3.98 kg ai/ha to 4.10 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: 0.025, 0.025, 0.116 mg/kg.

In sweet pepper, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 8) were: 0.048, 0.055, 0.063, 0.070, 0.073, 0.082, 0.136, and 0.232 mg/kg.

Application rates for these trials ranged from 3.84 kg ai/ha to 410 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: 0.030, 0.034, 0.041, 0.045 (2), 0.050, 0.083, and 0.146 mg/kg.

In tomato, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 20) were: < 0.01 (3), 0.013, 0.023, 0.026, 0.029, 0.034, 0.042, 0.072, 0.074, 0.078, 0.087, 0.088, 0.094, 0.173, 0.198, 0.231, 0.269, and 0.273 mg/kg.

Application rates for these trials ranged from 3.64 kg ai/ha to 4.12 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01 (4), 0.014, 0.016, 0.018, 0.021, 0.026, 0.045, 0.046, 0.049, 0.054, 0.055, 0.061, 0.108, 0.132, 0.140, 0.168, and 0.169 mg/kg;

Noting that the GAP in the USA is for the fruiting vegetables crop group, which is equivalent to the Codex group fruiting vegetables, other than Cucurbits except sweet corn and mushroom, and that the residue data from sweet pepper, chilli pepper, and tomato are not significantly different by the Kruskal-Wallis test, the Meeting determined that the residues from the trials are similar and is estimating a group maximum residue level for fruiting vegetables, other than Cucurbits except sweet corn and mushroom based on the following scaled BSA residue data set: (n = 31): < 0.01 (4), 0.014, 0.016, 0.018, 0.021, 0.025, 0.025, 0.026, 0.030, 0.034, 0.041, 0.045 (3), 0.046, 0.049, 0.050, 0.054, 0.055, 0.061, 0.083, 0.108, 0.116, 0.132, 0.140, 0.146, 0.168, and 0.169 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg for BSA on fruiting vegetables, other than Cucurbits except sweet corn and mushroom; the HR is 0.17 mg/kg (from a single sample) and the STMR is 0.045 mg/kg.

Based on the maximum residue level of fruiting vegetables, other than Cucurbits except sweet corn and mushroom (0.3 mg/kg) and a dehydration factor of 7, the Meeting estimated a maximum residue level of 2 mg/kg for BSA in chilli pepper (dry), an HR of 1.2, and an STMR of 0.32.

Fate of residues during processing

High-temperature hydrolysis

The Meeting received a study investigating the high-temperature hydrolysis of fluensulfone, BSA, MeS, and TSA. Samples of aqueous buffered solutions were spiked with fluensulfone, BSA, MeS, or TSA at ca. 1 mg/L and put under conditions simulating pasteurisation (90 °C, pH 4, 20 min.); baking, brewing, boiling (100 °C, pH 5, 60 min); and sterilisation (120 °C, pH 6, 20 min.). Solutions were analysed by HPLC-MS/MS prior to and after processing. All four analytes were shown to be stable under all three conditions, with overall recoveries ranging from 87 to 118% of the initial concentration.

Residues after processing

The Meeting received data depicting the concentration/dilution of residues during processing of tomato into canned, juice, puree, paste, wet and dry pomace, peeled, and sun-dried processed commodities. Processed commodities were derived using simulated commercial practices. Of the three studies that were submitted, two were suitable for deriving processing factors (in one study, all residues were < 0.01 mg/kg). In those two studies, residues of fluensulfone were < 0.01 mg/kg in all samples and processing factors for the parent compound could not be derived.

Crop	Processed commodity	BSA processing factors	Best processing factor estimate (average)	STMR-P, mg/kg	HR-P, mg/kg
Tomato	RAC	--	--	STMR = 0.045	HR = 0.17
	Canned	0.33	0.33	0.015	0.056
	Dry pomace	6.6, 9.3, 17	11	0.50	1.9
	Peeled	0.33	0.33	0.015	0.056
	Sundried	1.67, 2	1.8	0.081	0.31
	Juice	0.67, 0.83	0.75	0.034	0.13
	Paste	1, 1, 3.54	1.8	0.081	0.31
	Puree	0.67, 1.38	1.0	0.045	0.17
	Wet pomace	0.66, 3, 4	2.6	0.12	0.44

Based on the maximum residue estimate for fruiting vegetables, other than Cucurbits except sweet corn and mushroom (0.3 mg/kg) and the processing factor of 1.8 for both dried tomato and tomato paste, the Meeting recommends a maximum residue level of 0.5 mg/kg for BSA in dried tomato and 0.5 mg/kg for BSA in tomato paste.

Residues in animal commodities

The Meeting has determined that residue definitions for compliance and dietary intake are not necessary for animal commodities and that residues in animal commodities are not expected.

RECOMMENDATIONS

Definition of the residue for compliance with the MRLs and dietary intake for plant commodities: *3,4,4-trifluorobut-3-ene-1-sulfonic acid (BSA)*. Note that for dietary intake, exposure estimates should be compared to the ADI and ARfD for fluensulfone, with no correction for molecular weight.

Definition of the residue for compliance with the MRLs and for dietary intake for animal commodities: *Not necessary.*

Commodity		Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P, mg/kg
CCN	Name	New	Previous		
VC 0045	Fruiting vegetables, Cucurbits	0.3	–	0.032	0.16
VO 0050	Fruiting vegetables, other than Cucurbits except sweet corn and mushroom	0.3	–	0.045	0.17
HS 0444	Peppers chilli, dried	2.1	–	0.32	1.2
VW 0448	Tomato paste	0.5	–	0.081	0.31
DV 0448	Tomato, dried	0.5	–	0.081	0.31

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of BSA were calculated for the 17 GEMS/Food cluster diets using STMRs/STMR-Ps estimated by the current Meeting. The ADI for fluensulfone is 0–0.01 mg/kg bw. The calculated IEDIs for BSA were 0–3% of the maximum fluensulfone ADI. The Meeting concluded that the long-term intakes of residues of BSA, when fluensulfone is used in ways that have been considered by the JMPR, are unlikely to present a public health concern.

Short-term intake

The International Estimated Short-Term Intakes (IESTI) of BSA were calculated for food commodities and their processed commodities using HRs/HR-Ps or STMRs/STMR-Ps estimated by the current Meeting. The ARfD for fluensulfone is 0.3 mg/kg bw. The calculated maximum IESTI for BSA was 7% of the fluensulfone ARfD for all commodities. The Meeting concluded that the short-term intake of residues of BSA, when fluensulfone is used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

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R-25455	Quistad, GB, La Mar, J and Bautisata, A	2010	A Metabolism Study with [^{14}C]MCW-2 (2 Radiolabels) using Lettuce PTRL West, Inc. 625-B Alfred Nobel Drive, Hercules, California 94547, USA Makhteshim Chemical Works PTRL West Project No. 1786W, R-25455 GLP, Not published
R-23322	Schick, M	2011	Photodegradation of [^{14}C]MCW-2 in Sterilized pH 7 Buffer by Artificial Sunlight. PTRL West, Inc. 625-B Alfred Nobel Drive Hercules, CA 94547. Makhteshim Chemical Works, Ltd. Report No.: Report no. 1843W-001, R-23322 GLP, Not published
R-23319	Shepler, K	2010	Hydrolysis of [^{14}C]MCW-2 (Fluensulfone) at pH 4, 7 and 9 PTRL West, Inc. 625-B Alfred Nobel Drive Hercules, CA 94547. Makhteshim Chemical Works, Ltd. PTRL West Report No. 1843-001, R-23319 GLP, Not published
R-23309	Weissenfield, M	2008	MCW-2: Determination of the melting point / melting range. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00347, R-23309 GLP, Not published

Code	Author	Year	Title, Institute, Report reference
R-23310	Weissenfield, M	2008	MCW-2: Determination of the boiling point / boiling range. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00358, R-23310 GLP, Not published
R-23312	Weissenfield, M	2008	MCW-2: Determination of the relative density. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00360, R-23312 GLP, Not published
R-23313	Weissenfield, M	2008	MCW-2: Determination of the vapour pressure. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00382, R-23313 GLP, Not published
R-23316	Weissenfield, M	2008	MCW-2: Determination of water solubility. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00415, R-23316 GLP, Not published
R-23321	Weissenfield, M	2008	MCW-2: Calculation of dissociation constant. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00527, R-23321 Not GLP, Not published
R-23310A	Weissenfield, M	2009	MCW-2: Determination of the melting point / melting range and the boiling point / boiling range. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C30773, R-23310A GLP, Not published
R-23313A	Weissenfield, M	2009	MCW-2: Henry's Law constant—Expert statement. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00516, R-23313A Not GLP, Not published
R-23317	Weissenfield, M	2009	MCW-2: Determination of the solubility in organic solvents. Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C00437, R-23317 GLP, Not published
R-23330	Weissenfield, M	2010	MCW-2 Technical: Determination of the Storage Stability (Shelf Life). Harlan Laboratories Ltd, Zelgliweg 1, 4452 Itingen, Switzerland. Makhteshim Chemical Works Ltd, Harlan Laboratories Study C66198, R-23330 (was R-23307) GLP, Not published
R-23489	Witte, A	2011	Validation of an analytical method for the determination of residues of MCW-2 and three metabolites in plant commodities (acidic, dry and fatty). CIP Chemisches Institut Pforzheim GmbH Makhteshim Chemical Works Ltd CIP Study Code: 10M03036-01-VMPL, R-23489 GLP, Not published.
R-28495	Witte, A	2011	Validation of an Analytical Method for the Determination of Residues of MCW-2 metabolite #3626 (methylsulfone) in water containing plant commodities CIP Chemisches Institut Pforzheim GmbH Makhteshim Chemical Works Ltd CIP Study Code: 10M04006-01-VMPL, R-28495 GLP, Not published.
R-28512	Witte, A	2011	Validation of an Analytical Method for the Determination of Residues of MCW-2 and three Metabolites in Food Stuff of Animal Origin CIP Chemisches Institut Pforzheim BmbH Schulberg 17, D-75175 Pforzheim, Germany Makhteshim Chemical Works Ltd Report 11M03036-01-VMAT, R-28512 GLP, Not published

FLUFENOXURON (275)

The first draft was prepared by Ms. Monique Thomas. Pest Management Regulatory Agency, Canada

EXPLANATION

Flufenoxuron is a benzoylurea insect growth regulator with high levels of acaricidal activity. Flufenoxuron kills pest mites and insects through interference with chitin production during cuticle development in mite and insect juvenile stages. Flufenoxuron has limited to no effect on adult mites and insects. It is registered for use in a variety of crops worldwide.

IDENTITY

ISO common name: Flufenoxuron

Chemical name

IUPAC: N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}-N'-(2,6-difluorobenzoyl)urea

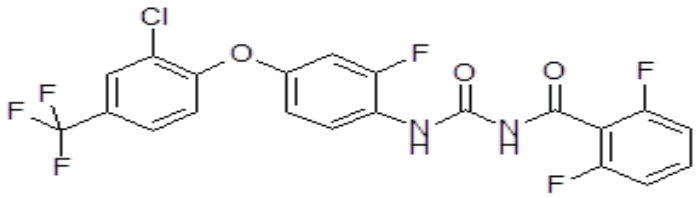
CAS: N-[[[4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl]amino]carbonyl]-2,6-difluorobenzamide

CAS Registry No: 101463-69-8

CIPAC No.: 470

Synonyms and Trade Name: WL115110, Cascade

Structural formula:



Molecular formula: $C_{21}H_{11}Cl\,F_6N_2O_3$

Molecular mass: 488.8 g/mol

Physical and Chemical Properties

Pure active ingredient, minimum purity 99.0%

Chemical/physical property	Results	Reference	Guidelines
Vapour Pressure (20 ºC)	6.52×10^{-9} mPa	FX-390-025 (2000/7000541)	EU Directive 91/414
Melting point	167–172 °C	FX-303-002	
Partition coefficient (25 ºC)	pH 4 : log P = 3.99 pH 7 : log P = 4.00 pH 9 : log P = 4.00	FX-301-002 (1988/7000758)	
Relative density (~22 ºC)	1.649	Kaestel 2001a, 2001/1019524	OECD Test Guideline 109
Henry's law constant (25 ºC)	7.46×10^{-6} Pa.m^3.mol^{-1}	FX-390-025 (2000/7000541)	EU Directive 91/414
Physical state, colour, odour	white, crystalline powder with a sourish odour.	Kaestel 2001b, 2001/1009097	EU Directive 91/414
Solubility in water [µg/L] (25 °C)	pH 4 : 1.86 pH 7 : 1.36 pH 9 : 3.69	Langner 1988a, FX-301-002 (1988/7000758)	

Chemical/physical property	Results	Reference	Guidelines
	Flufenoxuron is almost insoluble in water.		
Solubility in organic solvents [g/L] (20 °C[a])	n-heptane: < 0.01 n-octanol: 1.1 toluene: 3.5 dichloromethane: 16 methanol: 3.5 acetone: 83 ethyl acetate 55 acetonitrile: 6.62	Daum 2001a, FX-301-002 (2001/1017469)	OECD 105
Hydrolysis rate	Hydrolysis has been investigated at 50 °C at pH 5, 7 and 9. At pH 5 and 7: flufenoxuron is hydrolytically stable (half-life > 1 year). At pH 9 : > 87% of flufenoxuron was degraded after 5 days at 50 °C. Degradation was investigated at 60 °C and 70 °C, and half-life extrapolated at 25 °C was found to be 76 days.	Langner 1988a, FX-301-002 (1988/7000758)	
Photochemical degradation	Flufenoxuron decomposes under photolysis into 2,6-difluorobenzamide (maximum 84.5% at DAT 7), with a DT_{50} of 4.5 days under continuous irradiation at pH 7 and 22 °C. No counterpart metabolites were observed. Dark samples showed no degradation.	Hassink 2003a, 2003/1000986	
Quantum yield	$\Phi = 1.75 \times 10^{-3}$ for the radiolabelled active ingredient However the DT_{50} of the fluoroaniline radiolabelled active substance was poorly determined. For $290 < \lambda < 775$ nm : $\Phi = 2.2\ 10^{-3}$ mol. einstein^{-1}	Hassink 2003a, 2003/1000986	
Dissociation constant	pKa = 10.1	Camilleri & Langner 1986a, FX-311-002 (1986/7000994)	

[a] Purity 99.2%

Technical material; minimum purity 97.4%

Chemical/physical property	Results	Reference	Guidelines
Appearance	white, fine powder with a spicy odour.	Kaestel 2001c, 2001/1009099	
Relative density (20 °C [a])	1.57	Langer 1988a, FX-301-002 (1988/7000758)	

Chemical/physical property	Results	Reference	Guidelines
Flammability	Not flammable [b]	Van Helvoirt 1990a, FX-330-001 (1990/7001093)	EEC-Directive A-10
Auto-flammability	Not self-igniting [b]	Van Helvoirt 1990b, FX-330-002 (1990/7001094)	EEC-Directive A-16
Explosive properties	Not explosive [b]	Van Helvoirt & Cardinaals 1990a, FX-334-001 (1990/7001095)	EEC-Directive A-14
Oxidising properties	Not oxidising [b]	Van Helvoirt 1990c, FX-356-001 (1990/7001096)	EEC-Directive A-17

[a] Purity 97.4%
[b] Purity 97.6%

Formulation

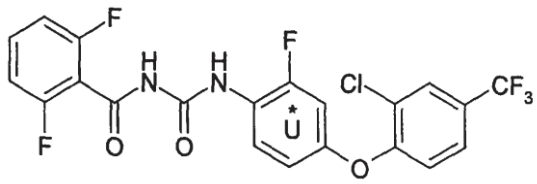
Flufenoxuron is commercially marketed as an emulsifiable concentrate containing 10% flufenoxuron.

Specification

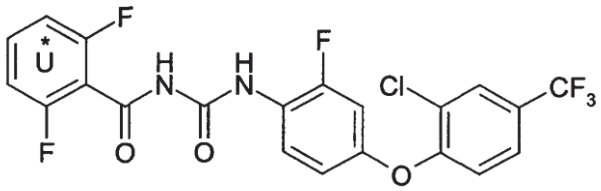
Flufenoxuron has not been evaluated by the Joint Meeting of Pesticide Specifications.

METABOLISM AND ENVIRONMENTAL FATE

The metabolism and distribution of flufenoxuron in plants and animals was investigated using ^{14}C-labelled test materials as shown below:

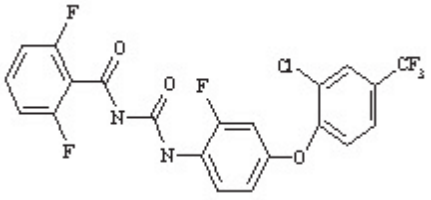


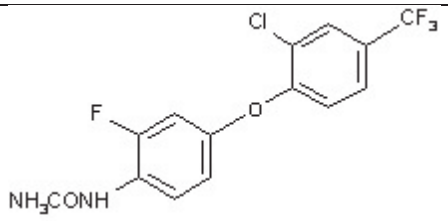
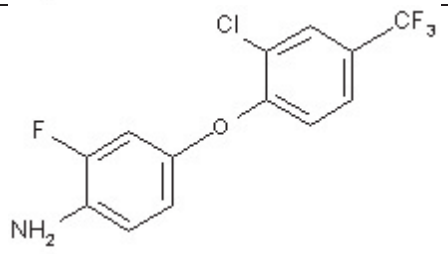
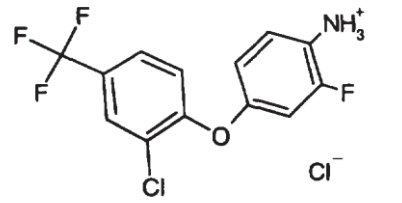
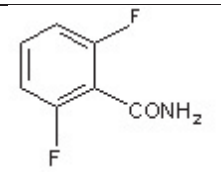
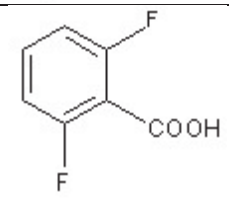
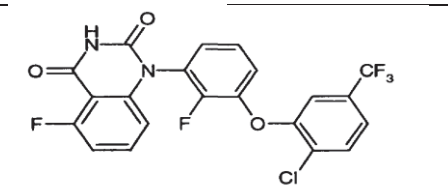
Fluoroaniline-U-^{14}C



Difluoroamide-U-^{14}C

Common chemical names, code names and structures of the parent and metabolites are captured below:

Code	*Structure*	*Occurrence*
Flufenoxuron WL115110 *N*-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}-*N*'-(2,6-difluorobenzoyl)urea		Rat Lactating goat Laying hen Grape Apple Tomato Chinese cabbage Soil Hydrolysis study

Code	*Structure*	*Occurrence*
Reg. No. 4064702 *N*-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}urea		Rat Laying hen Hydrolysis study
Reg. No. 241208 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluoroaniline		Rat Laying hen Hydrolysis study
Reg. No. 4064703 (chloride salt of Reg. No. 241208) 4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluoroaniline hydrochloride		Hydrolysis study
Reg. No. 102719 2,6 difluorobenzamide		Rat Hydrolysis study
Reg. No. 206925 2,6-difluorobenzoic acid		Rat Hydrolysis study
Reg. No. 4964847 1-{3-[2-chloro-5-(trifluoromethyl)phenoxy]-2-fluorophenyl}-5-fluoro-2,4(1H, 3H)-quinazolinedione		Hydrolysis study

Animal metabolism

The Meeting received information on the fate of [^{14}C]flufenoxuron in a lactating goat and laying hens. The lactating goat metabolism study was carried out with [^{14}C]flufenoxuron uniformly labelled at the fluoroaniline ring while the laying hen metabolism study was carried out with uniformly ^{14}C-labelled difluoroamide- and fluoroaniline-flufenoxuron. Metabolism in laboratory animals (rat) was summarised and evaluated by the WHO panel of the 2014 JMPR.

Lactating goat

The metabolism of [^{14}C]flufenoxuron was investigated in one lactating goat, weighing 73 kg, was dosed orally by gavage with 2-fluoroaniline-[U-^{14}C]-ring-labelled flufenoxuron once daily for 4 consecutive days at a dose level of 10 mg/day equivalent to 10 ppm in the diet. Milk production

ranged from 1.2–2.8 L/day. During the treatment period, milk was collected twice daily while urine and faeces were collected once daily. At sacrifice (within 24 hours after the last dose) samples of liver, kidney, muscle (hind leg and dorsal) and fat (deep body fat store along spine and renal) were collected.

The major route of elimination of the radioactivity was via the faeces which accounted for 18% of the total administered radioactivity (TAR); while urine accounted for 2.5% of the TAR and milk accounted for 8.3% of the TAR. Overall, the tissue burden was low, accounting for < 2% of the TAR. No further justification was provided for the low overall recovery of administered radioactivity (33% of the TAR).

The total radioactive residues (TRRs) were highest in fat (1.6 mg eq/kg), followed by liver (0.37 mg eq/kg), kidney (0.13 mg eq/kg) and muscle (0.076 to 0.1 mg eq/kg).

Table 1 Radioactive residue in organs and tissues

Organ/tissue	TRR [mg eq/kg]
Liver	0.37
Kidney	0.13
Skeletal muscle	
Hind leg	0.076
Dorsal	0.1
Deep body fat	1.6
Renal fat	1.6
Bile	0.26 mg eq/L
Whole blood	0.029 mg eq/L

Milk residues peaked on day 4 (average of 0.27 mg eq/L) with the highest concentrations of radioactivity detected in the cream fraction (accounting for 82–93% of the TRR in whole milk) and the lowest found in whey (1.3–5.7% of the TRR).

Table 2 ^{14}C-Residues in milk of goat dosed with 10 mg/day of 2-fluoroaniline-[U-^{14}C]-ring-labelled flufenoxuron

Day	Time (hours) [a]	TRR (mg eq/L)
1	7	0.27
2	23	0.09
	31	0.39
3	47	0.13
	55	0.23
4	71	0.16
	79	0.37
5	95	0.23

[a] Time after administration of first dose

Samples of tissues and milk were further analysed for determination of the distribution and composition of the total radioactivity. Liver and kidney samples were homogenised with ethyl acetate/methanol, muscle and fat samples were homogenised with dichloromethane while milk samples were mixed with potassium oxalate, ethanol and diethyl ether, all prior to partitioning with hexane and acetonitrile.

Aliquots of the acetonitrile phases of milk, liver, kidney, muscle and fat were mixed with appropriate amounts of the reference compound and subjected to HPLC/UV analysis.

Table 3 Characterisation of ^{14}C residues in tissues and milk of goat dosed with 2-fluoroaniline-[U-^{14}C]-ring-labelled flufenoxuron

Sample	% TRR Initial extraction efficiency	Acetonitrile/ hexane partition		Final recovery in acetonitrile fraction [%]
		% TRR in hexane fraction	% TRR in acetonitrile fraction	
Liver	93.4	3.8	88.5	82.8

Sample	% TRR Initial extraction efficiency	Acetonitrile/ hexane partition		Final recovery in acetonitrile fraction [%]
		% TRR in hexane fraction	% TRR in acetonitrile fraction	
Kidney	91.4	16.1	89.8	82.0
Muscle	66.2	9.8	114.5	63.5
Fat	99.8	1.5	115.3	107.4
Milk	98.3	0.0	81.1	81.1

Extraction of the samples collected recovered 64–107% of the TRR. HPLC/UV analysis of the extracts showed no evidence of cleavage of the flufenoxuron molecule or any metabolism of the parent substance in the goat. Hence, the parent compound remained intact with no other substances being detected in the analytical chromatograms.

The nature of the radioactivity in fat analysed after a 3–4 month storage period at –20 °C was examined by HPLC. No differences were noted in the metabolic profile.

Laying Hen

Study 1

Laying hens were dosed once daily for 14 consecutive days with flufenoxuron, uniformly labelled in the difluoroamide or fluoroaniline rings, at 13–14 ppm feed, equivalent to 0.78–0.85 mg/kg bw. Eggs were collected twice daily, in the morning before and in the afternoon after administration, whilst excreta was collected once daily. The animals were sacrificed approximately 23 h after the last dose and the liver, muscle and fat were collected and pooled per dose group. Liquid samples were measured directly by LSC while solid samples were combusted prior to analysis by LSC.

Excreta accounted for 72–78% of the TAR. Although no plateau was reached in eggs during the dosing period (14 days), the radioactivity recovered in eggs amounted to 1.0–1.3% of the TAR (0.5–0.8 mg eq/kg). Among all the tissues analysed, radioactive residues were highest in fat (5.0–5.3 mg eq/kg) followed by liver (0.6–1.1 mg eq/kg) and muscle (0.3–0.4 mg eq/kg). The total recovery of radioactivity was 82% and 77% in the difluoroamide-label and fluoroaniline-label groups, respectively.

Table 4 Recovery of radioactive residues in laying hens

Matrix	Difluoroamide label		Fluoroaniline label	
	% TAR	mg eq./kg	% TAR	mg eq./kg
Excreta	78.41		71.59	
Eggs	0.98		1.28	
Blood	0.02	0.113	0.40	1.269
Liver	0.11	0.577	0.24	1.056
GI-Tract (skin)	0.47	0.504	0.39	0.369
GI-Tract (contents)	0.06	0.252	0.06	0.213
Muscle	0.58	0.326	0.71	0.364
Adipose tissue	1.33	5.041	1.85	5.318
Subtotal organs	2.57		3.65	
Cage wash	0.13	–	0.11	–
Total	82.09	–	76.66	–

Extraction of radioactive residues from tissues and organs was initially performed with methanol, with the extractability ranging from 91–102% and 88–99% of the TRR for the difluoroamide- and fluoroaniline-labels, respectively. While the lowest extractability occurred with the liver from the fluoroaniline-label (88% of the TRR), microwave extraction of the liver post-extraction solid (PES) released another 8% of the TRR. Further characterisation according to polarity of residues was completed by partitioning with ethyl acetate/ water and acetonitrile/iso-hexane (for

fat, eggs and muscle) where the majority of the radioactivity was recovered in the ethyl acetate phase (93–101% and 82–104% of the TRR, difluoroamide- and fluoroaniline-label, respectively).

Table 5 Distribution of ^{14}C-residues in eggs and tissues

Label	Sample	TRR [mg/kg]	ERR [a] [mg/kg] (%TRR)	PES [b] [mg/kg] (%TRR)	Recovery [%] [c]
Difluoroamide	Egg	0.570	0.577 (101.3)	0.006 (1.0)	102.3
	Fat	5.041	5.088 (100.9)	0.011 (0.2)	101.1
	Liver	0.577	0.586 (101.5)	0.010 (1.7)	103.2
	Muscle	0.326	0.297 (91.3)	0.002 (0.7)	92.0
	Excreta [d]	4.082	4.065 (99.6)	0.018 (0.4)	100.0
Fluoroaniline	Egg	0.794	0.770 (97.1)	0.022 (2.8)	99.9
	Fat	5.318	5.258 (98.9)	0.038 (0.7)	99.6
	Liver	1.056	0.930 (88.1)	0.144 (13.6) [e]	101.7
	Muscle	0.364	0.341 (93.7)	0.014 (3.8)	97.5
	Excreta [d]	3.757	3.676 (97.8)	0.081 (2.2)	100.0

[a] ERR = Extracted Radioactive Residue (methanol)
[b] PES = Post-Extraction Solid
[c] Sum of all extracts and the residue
[d] Calculated value from ERR and PES
[e] Another 7.9% of the TRR was extracted by microwave treatment

For the difluoroamide-label, the parent was the only analyte identified in eggs, muscle, fat and liver ranging from 0.28 mg eq/kg (86.5% of the TRR, muscle) to 4.6 mg eq/kg (91.4% of the TRR, fat).

For the fluoroaniline-label, while the parent compound and the metabolite Reg. No. 4064702 were both identified in the eggs, muscle, fat and liver, the parent accounted for the majority of the TRRs (70–91%). The lowest level of parent was found in muscle with 0.30 mg eq/kg and the highest level in fat with 4.8 mg eq/kg. In eggs and liver, Reg. No. 4064702 was present at 0.10 mg eq/kg and 0.13 mg eq/kg (12.0% and 12.6% of the TRR), respectively. Reg. No. 4064702 was detected in muscle and fat as a minor metabolite amounting to 0.02 mg eq/kg and 0.05 mg eq/kg, respectively (5.5% and 1.0% of the TRR). The formate derivative of Reg. No. 241208 was released from the PES of liver after microwave treatment in the presence of formic acid/acetonitrile. The radioactivity associated with this derivative amounted to 0.04 mg eq/kg (3.3% TRR). The Meeting could not confirm whether the metabolite Reg. No. 241208 is an actual in-vivo metabolite or an artefact formed during microwave treatment.

Table 6 Identification of total radioactive residues in eggs and tissues

Label	Structure	Eggs [mg/kg] (%TRR)	Muscle [mg/kg] (%TRR)	Fat [mg/kg] (%TRR)	Liver [mg/kg] (%TRR)
Difluoroamide	Flufenoxuron	0.514 (90.3)	0.282 (86.5)	4.610 (91.4)	0.597 (103.5)
Fluoroaniline	Flufenoxuron	0.620 (78.2)	0.302 (82.9)	4.840 (91.0)	0.738 (69.9)
	Reg. No. 4064702	0.095 (12.0)	0.020 (5.5)	0.051 (1.0)	0.133 (12.6)

Label	Structure	Eggs [mg/kg] (%TRR)	Muscle [mg/kg] (%TRR)	Fat [mg/kg] (%TRR)	Liver [mg/kg] (%TRR)
	Reg. No. 241208	–	–	–	0.035 [a] (3.3)

[a] Amount of Reg. No. 241208 released from liver PES by microwave treatment

Study 2

Five groups (groups 1–5 and 7–10) of three laying hens each (White Leghorn hybrids, 1.4–2.1 kg) were dosed orally by gavage with 2-fluoroaniline-[U-^{14}C]-ring-labelled flufenoxuron once daily for seven consecutive days at a dose level of 10 mg/kg feed (corresponding to 0.5 mg/kg bw). One group of six untreated hens (group 6) served as a background control group.

Excreta from every group of hens was combined and sampled at 24 h intervals during administration. Eggs of individual hens were collected daily before each administration. After the final administration, before sacrifice, eggs and excreta were collected. Hens were sacrificed 22 hours after the final dosage or 2, 9, 16, and 34 days after the last dose to investigate the depuration behaviour of the flufenoxuron, liver, kidney, muscle (composite of breast and thigh muscle), gizzard (without lining and contents), heart, omental fat and skin were sampled. The content of the gizzard was added to the residual carcass.

On average, 26% of the TAR was excreta-related with eggs, sampled from 0–166 h after the first administration, accounting for 5% of the TAR. At sacrifice, the highest amount of radioactive residues was detected in fat (47% of the TAR), followed by skin (12% of the TAR), muscle (4% of the TAR), liver (2% of the TAR), kidney (0.3% of the TAR), heart and gizzard. The recovery of radioactivity amounted to 96% of the TAR.

Table 7 Balance of radioactivity (means of 15 hens) after seven daily doses of 0.5 mg/kg [^{14}C]-flufenoxuron sacrificed 22 hr after final dosage

Matrix	% TAR	mg eq./kg
Excreta	25.3	
Cage wash	0.6	
Eggs	4.7	6.0 egg yolks 0.02 egg whites
Liver	1.5	2.28
Kidney	0.3	1.26
Muscle	4.1	3.9
Fat	47.0	14.3
Skin	11.9	3.9
Heart	0.2	0.86
Gizzard		0.44
Total	95.6	

Table 8 Extractability of radioactivity from different organs of laying hens

Organ/tissue	TRR [mg/kg]	Acetone extract		Unextracted residue		% Recovery (extracted + unextracted)
		[mg eq/kg]	%TRR	[mg eq/kg]	%TRR	
Liver [a]	2.28	2.22	97.0	0.22	9.5	106
Kidney [a]	1.26	1.14	90.0	0.16	12.5	102
Muscle	0.38	0.38	102.0	0.03	8.1	110
Gizzard	0.44	0.41	94.2	0.05	11.7	106
Heart	0.86	0.83	96.5	0.09	10.2	107

Organ/tissue	TRR [mg/kg]	Acetone extract		Unextracted residue		% Recovery (extracted + unextracted)
		[mg eq/kg]	%TRR	[mg eq/kg]	%TRR	
Fat	14.3	12.94	90.5	0.03	0.2	91
Skin + adj. fat	3.9	3.58	91.9	0.02	0.6	92

[a] After incubation at 37 °C.

Extraction of the samples collected recovered > 90% of the TRR. HPLC/UV analysis of the extracts showed that flufenoxuron was not extensively metabolized and accounted for the majority of the radioactivity in egg yolks, liver, kidney, muscle, gizzard and heart while it was the only compound detected in fat and skin. Hydrolysis of the benzoyl urea bond resulted in the formation of fluoroaniline-label specific minor metabolites Reg. No. 4064702 and Reg. No. 241208.

The metabolite Reg. No. 4064702 was detected in yolks, liver, kidney, muscle, gizzard, and heart at 6–22% of the TRR. The minor metabolite Reg. No. 241208 was only detected in liver and kidney (≤ 4% of the TRR). The Meeting noted that liver and kidney were the only matrices that were incubated for 16 hours at 37 °C in 0.07 M phosphate buffer at pH 7.5 prior to extraction. However, the Meeting could not confirm that this metabolite is an artefact of the analytical procedure.

Additionally, one to three unknown radioactive fractions in yolks, liver and kidney extracts were detected (all below 10% of the TRR). In liver, three unknown fractions were characterized that were less polar than the reference items. The unknown fraction from yolks and kidney had a similar TLC-behaviour.

Table 9 Identification of total radioactive residues in eggs and tissues (%TRR)

Identity	Yolks	Liver	Kidney	Muscle	Gizzard	Heart	Fat	Skin
Flufenoxuron	84.9	66.3	59.6	90.4	89.5	90.3	98.2	97.2
REG. NO. 4064702	6.3	10.4	21.6	9.3	10.2	9.3	n.d.	n.d.
REG. NO. 241208	n.d.	3.7	2.5	n.d.	n.d.	n.d.	n.d.	n.d.
Total Identified	91.2	80.4	83.7	99.7	99.7	99.6	98.2	97.2
Total characterized (number of fractions)	8.8 (1)	2.9–7.6 (3)	8.9 (1)	–	–	–	–	–
Total Unidentified	–	4.0	7.4	0.3	0.3	0.4	1.8	2.8
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

The depuration study indicated that the radioactivity in egg yolks and muscle decreased steadily up to day 34. In kidney and liver, the decrease in radioactivity was more prominent from day 16 to day 34 of the depuration phase yet in fat, the decrease in radioactivity occurred most rapidly from day 2 to day 9 and from day 16 to day 34. These results demonstrated that radioactive residues are not retained in eggs, organs and tissues after cessation of dosing.

Overview of metabolism in livestock

In the lactating goat metabolism study, the parent flufenoxuron remained intact and was the only residue identified in milk and tissues.

In the laying hen metabolism studies, while flufenoxuron was the predominant residue in eggs and organs/tissues, cleavage of the benzoyl urea bond was observed to a limited extent resulting in the formation of minor metabolites Reg. No. 4064702 (eggs and tissues) and Reg. No. 241208 (liver and kidney).

Plant metabolism

Metabolism studies on tomato, apple, grape and Chinese cabbage were made available to the Meeting.

Grape

Grape-vine plants, variety Muller-Thurgau, grown outdoor and protected with plastic covers after application, were separately treated with [difluorobenzamide-U-^{14}C]- and [fluoroaniline-ring-U-^{14}C]flufenoxuron formulated as flowable concentrate formulations. Two foliar sprays were made during fruit development at a rate of 0.04 kg ai/ha/application with a 40-day retreatment interval. Mature samples of stalks and fruit (from grape clusters) were collected 28–29 days after last treatment (DAT), while leaves were collected at 15 DAT (immature) and 28–29 DAT (mature).

Total radioactive residues (TRRs) in leaves from the applications using difluorobenzamide-label were 2.7 mg eq/kg at 15 DAT and declined to 1.8 mg eq/kg at 29 DAT (Table 10). TRRs in mature fruit and stalks (29 DAT) were 0.014 mg eq/kg and 0.16 mg eq/kg, respectively. TRRs in leaves from applications using the fluoroaniline-label declined from 2.3 mg eq/kg at 15 DAT 1.4 mg eq/kg at 28 DAT. TRRs in mature fruit and stalks (28 DAT) were 0.012 mg eq/kg and 0.11 mg eq/kg, respectively. Overall, the distribution of radioactivity was relatively similar among both radiolabels.

Homogenized samples of fruit, leaf and stalk samples were extracted three times with methanol (MeOH) and twice with water. After each extraction step, the liquid phase was separated from the post extraction solid (PES) by centrifugation. The extracts and the dried PES were analysed by combustion for the determination of the residual radioactive residues. Aliquots of the MeOH extracts were evaporated to dryness, reconstituted in water and partitioned three times with hexane followed by three partition steps of the remaining aqueous phase with ethyl acetate. Aliquots of the organic and aqueous phases were analysed by LSC. Residues were identified by reverse-phase HPLC-UV and the identity of parent flufenoxuron was confirmed by HPLC with a Polymeric Reversed Phase (PRP-1) column.

As reported in Tables 10 and 11, approximately 95–97% of the TRR (0.012–2.6 mg eq/kg) was extracted from the grape matrices for both radiolabels. In all fruit, leaf and stalk samples (both labels), parent flufenoxuron was the only compound identified at 50–97% of the TRR (0.007–2.2 mg eq/kg). Polar unknowns comprised up to 40–46% of the TRR in mature grape samples (0.005–0.006 mg eq/kg) for both radiolabels. Unextracted residues in all leaf, fruit and stalk samples comprised ≤ 5% of the TRR (< 0.11 mg eq/kg), resulting in overall accountabilities of 99–100%.

The only metabolic reaction observed in grape matrices was the breakdown of flufenoxuron to mainly polar metabolites.

Table 10 Total radioactive residues (TRR) in grape matrices following two foliar applications of [^{14}C]-flufenoxuron at 0.08 kg ai/ha/season

Matrix	DAT (days)	TRR [a] (mg eq/kg)	Distribution of radioactive residues							
			MeOH		Water		Extracted radioactivity [b]		PES [c]	
			Mg eq/kg	% TRR	Mg eq/kg	% TRR	Mg eq/kg	% TRR	Mg eq/kg	% TRR
[difluorobenzamide-U-^{14}C]flufenoxuron										
Immature Leaves	15	2.673	2.551	95.4	0.022	0.8	2.573	96.2	0.100	3.7
Mature Leaves	29	1.819	1.763	96.6	0.011	0.6	1.774	97.2	0.045	2.5
Mature Fruit	29	0.014	0.014	95.8	< 0.0005	0.8	0.014	96.6	< 0.0005	3.4
Mature Stalks	29	0.163	0.17	96.3	0.001	0.5	0.158	96.8	0.005	3.2
[fluoroaniline-ring-U-^{14}C]flufenoxuron										
Immature Leaves	15	2.285	2.153	94.2	0.023	1.0	2.176	95.2	0.108	4.7
Mature Leaves	28	1.424	1.353	95.0	0.012	0.8	1.365	95.8	0.059	4.2
Mature Fruit	28	0.012	0.012	94.3	< 0.0005	0.8	0.012	95.1	0.001	4.9
Mature Stalks	28	0.106	0.100	94.5	0.001	0.8	0.101	95.3	0.005	4.7

[a] TRR = sum of extracted and unextracted radioactivity (PES)
[b] Methanol extract and water extract combined
[c] PES = post extraction solids (solids remaining after extraction)

Table 11 Summary of identified and characterized radioactivity extracted from [difluorobenzamide-U-^{14}C]-flufenoxuron -treated immature and mature leaves, grapes and stalks

Compound	Leaves (15 DAT)		Leaves (29 DAT)		Grapes (29 DAT)		Stalk (29 DAT	
	Mg eq/kg	%TRR	Mg eq/kg	%TRR	Mg eq/kg	%TRR	Mg eq/kg	%TRR
Flufenoxuron	2.305	86.2	1.763	96.9	0.007	49.7	0.157	96.3
Characterised [a]	0.269	9.9	0.011	0.6	0.006	46.9	0.001	0.5
Total extracted [b]	2.574	96.1	1.774	97.5	0.014	96.6	0.158	96.8
Total unextracted	0.100	3.7	0.045	2.5	< 0.001	3.4	0.005	3.2
Accountability [c]	2.674	99.8	1.819	100.0	0.014	100.0	0.163	100.0

[a] Total characterised consisted of polar unknowns, each accounting for <10% of the TRR and < 0.005 mg eq/kg
[b] Total extracted = MeOH and Aqueous extracts
[c] Accountability = (total extracted + total unextracted)/TRR

Table 12 Summary of identified and characterized radioactivity extracted from [U-Aniline-^{14}C]-flufenoxuron treated immature and mature leaves, grapes and stalks

Compound	Leaves (15 DAT)		Leaves (29 DAT)		Grapes (29 DAT)		Stalk (29 DAT)	
	Mg eq/kg	%TRR	Mg eq/kg	%TRR	Mg eq/kg	%TRR	Mg eq/kg	%TRR
Flufenoxuron	2.153	94.2	1.353	95.0	0.007	54.6	0.100	94.5
Characterised [a]	0.023	1.0	0.012	0.8	0.005	40.5	0.001	0.8
Total extracted [b]	2.176	95.2	1.365	95.8	0.012	95.1	0.101	95.3
Total unextracted	0.108	4.7	0.059	4.2	0.001	4.9	0.005	4.7
Accountability [c]	2.284	99.9	1.424	100.0	0.013	100.0	0.106	100.0

[a] Total characterised consisted of polar unknowns, each accounting for < 10% of the TRR and < 0.005 mg/kg
[b] Total extractable = MeOH and Aqueous extracts
[c] Accountability = (total extracted + total unextracted)/TRR

Apple

Flufenoxuron uniformly labelled in the fluoroaniline ring, formulated as a dispersible concentrate, was sprayed on 10 apple trees (var. Cox's Orange Pippin), maintained in glasshouses. The trees were treated during fruit development, when fruit was approximately 20 mm in diameter, with a single application at a rate of 0.1 kg ai/hL. Samples of immature fruit were harvested 0 days (4 h post-treatment) and 46 days after treatment (DAT), and mature fruit samples were collected at 99 DAT.

Immediately after harvest, all fruit samples (0, 46 and 99 DAT) were washed sequentially with acetonitrile (ACN) and hexane. Total radioactivity was determined in the washes and the fruit by combustion/LSC. At DAT 99 four additional apples were harvested; two of these were not washed and used for autoradiography while two other apples were washed as described above and separated into peel, pulp and seeds prior to analysis.

For the characterization/identification of residues, only the surface washes from the 0 and 99 DAT samples were prepared. Washed fruit samples were extracted three times with ACN:water (7:3, v/v) and centrifuged. The supernatants were combined and partitioned twice with dichloromethane (DCM). The DCM fraction was dried under a stream of nitrogen, and resuspended in DCM for TLC analysis. For HPLC-UV analysis, the DCM was removed under nitrogen and the residue was resuspended in ACN:water (7:3, v/v). The identity of parent flufenoxuron was confirmed by HPLC with a Polymeric Reversed Phase (PRP-1) column.

Total radioactive residues (TRRs) in immature fruit were 2.6 mg eq/kg (0 DAT) and declined to 0.16 mg eq/kg (46 DAT) and 0.06 mg eq/kg (99 DAT), likely due to the increasing size of the fruit as it matured (Table 13). The surface washes accounted for 77–96% of the TRRs with unextracted residues comprising 0.3–2.5% of the TRR (0.001–0.008 mg eq/kg), resulting in accountabilities of 93–100%. Parent flufenoxuron was the only compound identified in the surface washes (74–93% of

the TRRs; 0.043–2.4 mg eq/kg) and fruit extracts (3–16% of the TRRs; 0.01–0.08 mg eq/kg). There were no residues other than the parent that were identified in the apple samples.

For the two apples separated into peel, pulp and seeds and those subjected to autoradiography, the same trend was observed whereby the majority of the radioactivity remained on the peel with limited translocation of the TRRs into the pulp and the seeds.

Table 13 Total radioactive residues (TRR) in apples following a single foliar application of [^{14}C]-flufenoxuron at 100 mg ai/L

Matrix	DAT	TRR [a] (mg/kg)	Distribution of radioactive residues					
			Surface wash (ACN+ Hexane)		Fruit Extract		PES [b]	
			mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
Immature fruit	0	2.551	2.457	96.3	0.094	3.7	0.008	0.3
Immature fruit	46	0.163	0.146	89.4	0.017	10.6	0.000	0.0
Mature fruit	99	0.055	0.043	77.0	0.013	23.0	0.001	2.5

[a] TRR = sum of extracted and unextracted radioactivity (PES)
[b] PES = post extracted solids (solids remaining after extraction)

Table 14 Summary of characterization and identification of ^{14}C-residues in apple fruit following a single foliar application of [U-Aniline-^{14}C]-flufenoxuron at 100 mg ai/L

	Immature Fruit (0 DAT)		Mature Fruit (99 DAT)	
	mg eq/kg	%TRR	mg eq/kg	%TRR
Flufenoxuron	2.462	96.5	0.054	90.9
Total extracted [a]	2.551	100.0	0.054	90.9
Total unextracted	0.008	0.3	0.001	2.5
Accountability [b]	2.559	100.3	0.055	93.4

[a] Total extracted = surface wash + fruit extract
[b] Accountability = (total extracted + total unextracted)/TRR

Tomato

[U-Aniline-^{14}C]flufenoxuron mixed in approximately equal proportions with [aniline-^{15}N] and formulated as an emulsifiable concentrate, was applied as a single broadcast foliar application to tomato plants (var. Moneymaker) maintained in an outdoor uncovered enclosure. The application was made during fruit development at a rate of 0.125 kg ai/ha and tomato fruit was harvested at 0 and 28 days after treatment (DAT).

Tomato fruit samples were surface washed with ACN:water (7:3, v/v) five times prior to extraction. The washed fruit were homogenized and extracted once with ACN:water (7:3, v/v) and filtered. The surface washes and extracts were diluted with water and partitioned three times with DCM. The organic phase was concentrated, then analysed by thin-layer chromatography (TLC). Radioactivity in surface washes and extracts were determined by LSC while the unextracted solid residues were subjected to combustion analysis.

Total radioactive residue (TRR) in/on tomato fruit declined from 0.38 mg eq/kg on day 0, to 0.17–0.2 mg eq/kg by day 28 (Table 15). The total extracted residues (surface washes and fruit extracts) from 0 DAT to 28 DAT, accounted for 94–99% of the TRR (0.16–0.38 mg eq/kg), mainly from the surface wash (≥ 94% of the TRRs). Unextracted residues comprised 1.1–5.8% of the TRR (0.004–0.012 mg eq/kg). Only sample II (28 DAT; 0.2 mg eq/kg) underwent identification/characterization of TRRs. Radio- TLC of the extracted radioactivity showed the parent flufenoxuron as the only identified residue, accounting for 91% of the TRR (0.18 mg eq/kg).

Table 15 Total radioactive residues (TRR) in tomato fruit following a single application of [U-Aniline-^{14}C]-flufenoxuron at 0.125 kg ai/ha

Matrix	DAT	TRR [a] (mg eq/kg)	Distribution of radioactive residues					
			Surface wash (ACN+ Water)		Fruit Extract		PES [b]	
			mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
Tomato Sample	0	0.38	0.374	98.0	0.003	0.9	0.004	1.1
Tomato Sample I	28	0.17	0.160	95.4	0.001	0.5	0.007	4.1
Tomato Sample II	28	0.20	0.185	93.8	0.001	0.4	0.012	5.8

[a] TRR = sum of extracted and unextracted radioactivity (PES)
[b] PES = post extracted solids (total unextracted)

Table 16 Summary of characterization and identification of ^{14}C residues in tomato fruit following a single foliar application of [U-Aniline-^{14}C]-flufenoxuron at 0.125 kg ai/ha

Compound	Tomato Sample (0 DAT)		Tomato Sample I (28 DAT)		Tomato Sample II (28 DAT)	
	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
Flufenoxuron	NR	NR	NR	NR	0.182	91.0
Total Extracted	0.376	98.9	0.164	95.9	0.188	94.2
Total Unextracted	0.004	1.1	0.007	4.1	0.012	5.8
Accountability [a]	0.380	100	0.171	100	0.200	100

NR = Not reported. Identification/Characterization of residues was only performed on the 28 DAT Tomato Sample II.
[a] Accountability = Total extracted + total unextracted

Chinese cabbage

[U-Aniline-^{14}C]flufenoxuron mixed in approximately equal proportions with [aniline-^{15}N] flufenoxuron, formulated as an emulsifiable concentrate, was applied as a single foliar application at a rate equivalent to 0.10 kg ai/ha to Chinese cabbage plants (grown outdoors) during leaf development. Cabbage plants were harvested at 0 and 28 days after treatment (DAT).

Samples of wrapper leaves were surface washed with ACN:water (7:3, v/v) five times prior to extraction. The washed leaves were homogenized, extracted (once for 0 DAT samples and twice for 28 DAT samples) with ACN:water (7:3, v/v) and filtered. The surface washes and extracts were diluted with water and partitioned three times with DCM. The organic phase was concentrated, then analysed by thin-layer chromatography (TLC). Radioactivity in surface washes and extracts were determined by LSC while the unextracted solid residues were subjected to combustion analysis.

Total radioactive residue (TRR) in/on cabbage wrapper leaves declined from 5.5–7.0 mg eq/kg (average 6.3 mg eq/kg) on day 0, to 0.33–0.36 mg eq/kg (average 0.35 mg eq/kg) by day 28. The total extracted residues (surface washes and extracts from the washed leaves) accounted for 94–97% of the TRR (0.32–6.8 mg eq/kg). However, at 0 DAT, the surface wash represented the majority of the extractable residues while at the 28 DAT, the leaf extracts accounted for much of the extractable radioactivity. Unextracted residues comprised 2.6–5.9% of the TRR (0.01–0.21 mg eq/kg). Only the 28-DAT sample (0.36 mg eq/kg) underwent identification/characterization of residues. Radio- TLC of the extracted radioactivity showed the parent flufenoxuron as the only identified residue, accounting for 93% of the TRR (0.34 mg eq/kg).

Table 17 Total radioactive residues (TRR) in Chinese cabbage leaves following a single foliar application of [U-Aniline-^{14}C]-flufenoxuron at 0.1 kg ai/ha

Matrix	DAT	TRR [a] (mg eq/kg)	Distribution of radioactive residues					
			Surface wash (ACN+ water)		Leaf Extract		PES [b]	
			mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% T2.8RR
Cabbage	0	6.3	5.3	84.0	0.8	13.2	0.2	2.8
Cabbage	28	0.35	0.07	18.9	0.27	75.9	0.01	5.2

All values reported as mean of replicate samples
[a] TRR = sum of extracted and unextracted radioactivity (PES)
[b] PES = post extracted solids (total unextracted)

Table 18 Summary of characterization and identification of ^{14}C residues in Chinese cabbage leaves following a single foliar application of [U-Aniline-^{14}C]-flufenoxuron at 0.1 kg ai/ha

Compound	Cabbage sample (0 DAT)		Cabbage sample (28 DAT)	
	mg eq/kg	% TRR	mg eq/kg	% TRR
Flufenoxuron	NR	NR		92.5
Total Extracted		97.2		94.8
PES		2.8		5.2
Accountability [a]		100		100

NR = Not reported. Identification/Characterization of residues was only performed on cabbage (28 DAT) sample.
[a] Accountability = Total extracted + PES

Overview of metabolic pathway in plants

The grape, apple, tomato and cabbage metabolism studies indicated that parent flufenoxuron was the only residue identified in all the tested primary crop matrices, and was found at > 90% of the TRR except grapes, where parent accounted for 50% of the TRR. No other metabolites were identified and no other residues were characterized (other than polar unknowns). The metabolism data (including autoradiography of the apple samples) indicated that the majority of radioactivity remained on the leaves or surface of the fruit, with limited translocation.

Environmental fate

The Meeting received information on, aerobic and anaerobic degradation in soil, photolysis on soil and pH based degradation. In conformance with the FAO manual 2009, only studies on aerobic degradation in soil were considered for the current evaluation. The fate and behaviour of flufenoxuron in the environment was investigated using amide-[U-^{14}C]-ring-labelled-flufenoxuron.

Study 1

The rate of aerobic degradation of flufenoxuron in three soils at a temperature of 20 °C was investigated [Goodyear and Gross, 2001, ENV 01-030]. Samples of test soils (50 g dry weight equivalent at 45% maximum water holding capacity (MWHC)), sieved to 2 mm were dispensed into flasks and treated with amide-[U-^{14}C]-ring-labelled-flufenoxuron at a nominal rate of 0.15 µg ai/g, corresponding to a field application rate of 150 g ai/ha. The treated soils were incubated in the dark at 20 ± 2 °C with moistened carbon dioxide free air drawn through the flasks for up to 120 hours. Volatiles in effluent air were trapped successively in ethanediol, 2% paraffin in xylene and 2 M sodium hydroxide. Samples were taken at 0, 2, 7, 14, 30, 59, 90 and 120 days after treatment (DAT). Trapping solutions were sampled and replaced on the same days.

Flufenoxuron was the only residue present at each sampling interval. The flufenoxuron concentration decreased steadily in all three soil types. At day 0, flufenoxuron represented > 99% TAR and decreased to 22–52% TAR after 120 days of incubation.

Table 19 Recovery of radioactivity and distribution of metabolites after application of amide-^{14}C-flufenoxuron to Chapel Hill Farm soil and incubation under aerobic conditions [%TAR]

Soil Name				SK 960087		
Source				Chapel Hill Farm, Empingham, Rutland, UK		
UK Particle Size Distribution Sand % (2000–63 µm) Silt % (63–2 µm) Clay % (< 2 µm) Textural Class				 33 35 32 Clay loam		
Organic carbon (%)				2.7		
Organic matter (%)				4.7		
pH in H_2O				8.0		
pH in 1 M KCl				7.2		
CEC (mEq/100 g)				19.6		
Water Holding Capacity pF0 (0.001 bar)%				56.6		
Water Holding Capacity pF2.5 (0.33 bar)%				25.0		
Microbial biomass (µg C/g) —start of study —end of study				 526.5 500.1		
Day	Flufenoxuron	Unresolved	CO_2	Other volatiles	Water soluble	Total % recovery
0	100.0	0.4	NA	NA	ND	102.7
2	95.1	0.7	0.3	ND	ND	99.4
7	91.1	0.3	1.4	ND	ND	97.6
14	89.5	ND	2.8	ND	ND	100.5
30	83.1	ND	5.5	ND	ND	97.9
59	70.2	0.3	10.1	ND	1.7	97.2
90	58.6	0.2	18.5	ND	2.3	98.6
120	51.6	0.4	23.2	ND	2.1	98.5

ND =Not detected
NA = Not applicable
CO_2 is the sum of the radioactivity in the 2M sodium hydroxide traps
Other volatiles is the sum of the radioactivity in the ethanediol and 2%paraffin in xylene traps

Table 20 Recovery of radioactivity and distribution of metabolites after application of amide-^{14}C-flufenoxuron to Newhaven soil and incubation under aerobic conditions [%TAR]

Soil Name				SK 15556090		
Source				Newhaven Cottage, Hartington Upper Quarter, Derbyshire, UK		
UK Particle Size Distribution Sand % (2000–63 µm) Silt % (63–2 µm) Clay % (< 2 µm) Textural Class				 23 57 20 Clay loam		
Organic carbon (%)				4.5		
Organic matter (%)				7.8		
pH in H_2O				6.7		
pH in 1 M KCl				6.2		
CEC (mEq/100 g)				17.4		
Water Holding Capacity pF0 (0.001 bar)%				107.7		
Water Holding Capacity pF2.5 (0.33 bar)%				48.5		
Microbial biomass (µg C/g) —start of study —end of study				 604.8 654.1		
Day	Flufenoxuron	Unresolved	CO_2	Other volatiles	Water soluble	Total %recovery
0	101.0	0.5	NA	NA	ND	103.2
2	96.5	0.7	1.4	ND	ND	101.9
7	85.6	0.3	5.4	ND	1.1	100.8
14	69.1	ND	13.3	ND	0.6	97.1
30	56.2	0.1	21.9	ND	1.5	97.4

Soil Name				SK 15556090		
Source				Newhaven Cottage, Hartington Upper Quarter, Derbyshire, UK		
59	37.6	0.2	34.7	ND	1.8	98.4
90	24.7	0.1	46.0	ND	2.2	99.5
120	22.0	0.1	52.5	ND	1.9	101.6

ND =Not detected
NA = Not applicable
CO_2 is the sum of the radioactivity in the 2 M sodium hydroxide traps
Other volatiles is the sum of the radioactivity in the ethanediol and 2%paraffin in xylene traps

Table 21 Recovery of radioactivity and distribution of metabolites after application of Amide-^{14}C-flufenoxuron to Baylam soil and incubation under aerobic conditions [%TAR]

Soil Name				PT 103		
Source				Baylam, Ipswich, Suffolk, UK		
UK Particle Size Distribution Sand % (2000–63 µm) Silt % (63–2 µm) Clay % (< 2 µm) Textural Class				 71 14 15 Sandy loam		
Organic carbon (%)				1.4		
Organic matter (%)				2.4		
pH in H_2O				5.5		
pH in 1 M KCl				4.9		
CEC (mEq/100 g)				8.3		
Water Holding Capacity pF0 (0.001 bar)%				47.6		
Water Holding Capacity pF2.5 (0.33 bar)%				16.2		
Microbial biomass (µg C/g) —start of study —end of study				 434.9 226.1		
Day	Flufenoxuron	Unresolved	CO_2	Other volatiles	Water soluble	Total %recovery
0	99.1	0.5	NA	NA	ND	100.6
2	96.2	0.7	1.2	ND	ND	101.8
7	82.1	0.2	6.1	ND	0.8	98.4
14	73.4	0.2	10.8	ND	0.7	98.1
30	60.3	0.2	19.5	ND	1.5	100.2
59	50.5	0.2	24.3	ND	1.8	96.4
90	46.8	0.3	30.1	ND	1.5	98.7
120	38.3	0.1	36.4	ND	ND	97.4

ND =Not detected
NA = Not applicable
CO_2 is the sum of the radioactivity in the 2M sodium hydroxide traps
Other volatiles is the sum of the radioactivity in the ethanediol and 2% paraffin in xylene traps

Table 22 Dissipation times of flufenoxuron

Parameter	SK 960087	SK 15556090	PT 103
DT_{50} (days)	124	36	64
DT_{90} (days)	432	191	449
R2 (correlation coefficient)	0.998	0.997	0.997

Study 2

The aerobic degradation rate of 2-fluoroaniline-[U-^{14}C]-ring-labelled-flufenoxuron was investigated in two types of soils, while the degradation of the flufenoxuron-derived soil metabolite, ^{14}C-Reg. No. 4064702, was investigated in four different soils [Stephen and Ebert, 2003, 83303]. Samples of test soils (40% MWHC) were dispensed into glass bottles, treated at a nominal rate of 0.05 mg ai/kg,

corresponding to a field application rate of 40 g ai/ha, and incubated in the dark at 20 ± 2 ºC. Samples were taken at 0, 3, 7, 14, 30, 57, 91 and 119 days after treatment (DAT).

Table 23 Soil characteristics

Soil Name	Bruch West	Li35B	LUFA2.2	LUFA 3.
Particle Size (Pipette method) (%)				
2000 to ≥ 1000 µm	0.2	1.0	0.5	0.5
1000 to ≥ 500 µm	2.7	6.5	2.3	2.1
500 to ≥ 250 µm	16.3	29.6	25.4	5.2
250 to ≥ 100 µm	39.0	30.0	45.6	26.8
100 to ≥ 50 µm	17.8	8.6	6.7	22.1
50 to ≥ 2µm	23.1	17.0	1504	37.9
< 2 µm	0.8	7.4	4.1	5.4
Textural Class	Loamy sand	Loamy Sand	Loamy sand	Sandy loam
TOC (Coulometric titration) (%)	2.29	0.89	2.38	2.38
TC (Coulometric titration) (%)	3.90	0.90	2.38	4.00
pH in H_2O	7.0	7.1	6.6	8.1
pH in CaCl	7.8	6.3	5.9	7.4
CEC (mval Ba/100 g dry weight)	14.0	7.4	9.7	19.6
Water Holding Capacity (g/100 g dry weight)	30.4	27.7	39.4	42.8
Total Nitrogen (%)	0.16	0.10	0.19	0.22
Ammonium-N (Ion chromatography) (mg/100 g dry weight)	0.3	0.3	0.5	0.4
Nitrate-N (Ion chromatography) (mg/100 g dry weight)	0.20	0.10	0.09	1.8
Microbial biomass (OxiTop method) (mg C/100 g dry weight)	30.2	16.2	36.1	67.8
Ratio Microbial biomass / TOC (calculated) (%)	1.3	1.8	1.5	2.8

The amounts of extractable residues, in both soils treated with radiolabelled flufenoxuron, decreased to ≤ 50% of the total applied radioactivity while the bound residues increased to 38.8–43.8% TAR. No formation of CO_2 was noted. Following treatment of four soils with the metabolite Reg. No. 4064702, less than 25.5% TAR was extractable after 119 days of incubation. The bound residues reached levels of 65–80% TAR at the end of the incubation period. In two of the soils, slow mineralization was observed, reaching 2–8%TAR at the end of incubation while in the other two soils, there was no evidence of CO_2 evolution.

When treated with radiolabelled flufenoxuron, the metabolite Reg. No. 4064702, representing the fluoroaniline moiety after cleavage of the flufenoxuron molecule, was identified by chromatographic comparison with the ^{14}C-labelled reference compound. The highest concentration of this metabolite was reached after 30 days of incubation, accounting for 4.1–8.3% TAR. Flufenoxuron decreased to 45.8–51.0% TAR in the soil after 119 days. While other peaks could be observed in the chromatograms at 119 DAT, all were below the limit of quantification (0.001 mg/kg). The DT_{50} was calculated to be in the range of 115–122 days (Table 24).

In all four tested soils treated with Reg. No. 4064702, the metabolite degraded relatively quickly reaching < 50% TAR after 57 days of incubation and 16–24% TAR after 119 days. According to the chromatograms of the extracts from sampling days 57, 91 and 119, two degradation products were detected and present at concentrations close to the LOQ. One of these appeared to be the metabolite Reg. No. 241208, DT_{50} values were in the range of 47–59 days (Table 24).

Table 24 Dissipation times of flufenoxuron and the metabolite Reg. No. 4064702

Analyte	Soil	DT_{50} (days)	DT_{90} (days)
Flufenoxuron [a]	Bruch West	122	407
	Li35B	115	381
Reg. No. 4064702 [b]	Bruch West	57	190
	Li35B	56	186
	LUFA 2.2	59	196
	LUFA 3A	47	156

[a] Degradation rates obtained using a 2 compartment model
[b] Degradation rates obtained using a 3 compartment model

Based on the findings of the soil aerobic degradation studies, the DT_{50} of flufenoxuron and the metabolite Reg. No. 4064702 were 124 days and 57 days, respectively, demonstrating persistence of the parent in soil yet limited persistence of the metabolite.

Residues in Rotational Crops

Neither confined crop rotation or field accumulation studies were submitted.

METHODS OF RESIDUE ANALYSIS

Analytical methods

The meeting received analytical method descriptions and validation data for flufenoxuron in plant and animal commodities and in soil and water. For the majority of the methods, residues of flufenoxuron are measured by HPLC-MS/MS with two specific mass transitions or with HPLC-UV at 254–260 nm for each analyte. All methods were validated at the determined LOQs, ranging from 0.01–0.05 mg/kg depending on the matrix. A summary of the analytical methods for plant and animal commodities and environmental media is provided below.

The applicability of the DFG S19 multi residue method was investigated using animal matrices (milk, meat, eggs), however, the results did not confirm sufficient applicability.

A number of scientific papers report the validation of the QuEChERS multiresidue method using GC-MS/MS for flufenoxuron in various plant commodities.

Table 25 Overview of flufenoxuron analytical methods for plant matrices

Method	Matrix	Analyte(s)	Extraction	Clean-up	Detection, LOQ	Reference
Enforcement method						
RLA 12675	Grapes, lettuce, tomatoes and tomato processing commodities	Flufenoxuron	DCM	Liquid/liquid partitioning with water/cyclohexane or aqueous acidic methanol/ cyclohexane.	HPLC-MS/MS 0.05 mg/kg	2003/1004358
	Grapes, tomatoes, wheat grain, wheat forage, wheat straw and rape seed	Flufenoxuron	DCM	Liquid/liquid partitioning with water/cyclohexane.	HPLC-MS/MS 0.05 mg/kg	2004/1000759 Independent laboratory validation
	Orange and melon	Flufenoxuron	DCM	Liquid/liquid partitioning with water/cyclohexane.	HPLC-MS/MS 0.05 mg/kg	2008/7012012 Independent laboratory validation
Data generation methods						

P1907-G	Apple, citrus, soya bean, wheat grain	Flufenoxuron CL 359882, CL 932338, CL 211558	methanol, water and HCl		HPLC-MS/MS 0.01 mg/kg	2010/1051669
Not specified	Tea Leaves	Flufenoxuron	Aqueous acetone	Liquid/liquid partitioning with hexane followed by ACN.	HPLC-UV 0.8 mg/kg	FX-790-025
Not specified	Infused tea	Flufenoxuron	Precipitation with acetone and lead acetate	Liquid/liquid partitioning with hexane.	HPLC-UV 0.8 mg/kg	FX-790-026
P1340G	Green tea	Flufenoxuron, CL 932338, CL 211558, CL 359882	Methanol/ water/HCl		HPLC-MS/MS 0.01 mg/kg	2007/300204
	Green tea	Flufenoxuron	Methanol/ water/HCl		HPLC-MS/MS 0.1 mg/kg	2008/1042807 Independent laboratory validation

Table 26 Overview of flufenoxuron analytical methods for animal matrices

Method	Matrix	Analyte(s)	Extraction	Clean-up	Detection, LOQ	Reference
Enforcement methods						
SAMS 458-1	Fat	Flufenoxuron	Warm acetone/hexane (20:80 v/v) and sodium sulphate	Partitioning with ACN and clean-up by RP HPLC.	HPLC-UV 0.01 mg/kg	FX-245-003
	Fat	Flufenoxuron	Methylene chloride and sodium sulphate	Clean-up by SPE and RP HPLC.	HPLC-UV 0.05 mg/kg	FX-245-009 Independent laboratory validation
SAMS 486-1	Milk	Flufenoxuron	Diethyl ether and hexane	Partitioning with ACN followed by clean up with NP HPLC.	HPLC-UV 0.1 µg/L	FX-245-004
	Milk	Flufenoxuron	Potassium oxalate and ethanol followed by diethyl ether and hexane	Partitioning with ACN followed by clean up with NP HPLC.	HPLC-UV 0.01 mg/kg	FX-245-008 Independent laboratory validation
Data generation methods						
DFG S 19	Milk, meat, eggs	Flufenoxuron	Aqueous acetone		HPLC-MS/MS 0.01 mg/kg	2002/5004112 (not sufficiently validated)
SAMS 457-2	Fat, whole blood, muscle, kidney, liver, bone marrow	Flufenoxuron	Sodium sulfate, hexane and ACN	Liquid/liquid partitioning and clean-up by NP or RP HPLC	HPLC-UV 0.03 mg/kg	FX-245-002 (1989/7000985)
SAMS 457-1	Liver	Flufenoxuron	Acetone/hexane (20:80 v/v) and sodium sulphate	Partitioning with water/ACN (20:80 v/v).	HPLC-UV LOQ not reported	FX-245-010
Not specified	Blood	Flufenoxuron	Warm acetone	Partitioning with hexane.	HPLC-UV LOQ not reported	FX-245-006
SAMS 492-1	Eggs	Flufenoxuron	Boiling acetone and hexane	Partitioning with ACN followed by clean-up with	HPLC-UV 0.01 mg/kg	FX-245-005

				NP HPLC.		
01791.PCC	Liver of poultry	REG. NO. 4064702	Acetonitrile	Partitioning with n-hexane and clean-up by RP semi-preparative HPLC	HPLC-UV 0.03 mg/kg	FX-705-006

Plant materials

Method RLA 12675 involves extraction of flufenoxuron residues from finely chopped fruit with dichloromethane. An aliquot of the extract is evaporated to dryness, reconstituted in cyclohexane, and then partitioned with water. An aliquot of the cyclohexane phase is taken, evaporated to dryness, reconstituted in acetonitrile:methanol:water (58:10:32, v/v/v), and analysed by LC-MS/MS using the positive ionization mode monitoring ion transitions *m/z* 498→158 (for quantitation) and *m/z* 498→141 (for confirmatory purposes).

The applicability of the method was confirmed in an independent laboratory by Schulz (2004, 2004/1000759) and Saha (2008, 2008/7012012). In both laboratories, parent flufenoxuron was analysed with a validated LOQ of 0.05 mg/kg (Table 27).

Table 27 Independent laboratory recovery results for method RLA 12675

Matrix	Fortification level [mg/kg]	No. of tests	Range of Recoveries [%]	Mean Recovery [%]	SD
Tomato	0.05	5	78–92	83	5.7
	0.5	5	78–88	82	4.3
Grapes	0.05	5	86–98	90	4.8
	0.5	5	87–93	90	2.7
Wheat grain	0.05	5	84–92	87	2.9
	0.5	5	79–87	83	3.2
Wheat forage	0.05	5	81–85	83	1.8
	0.5	5	84–89	86	1.8
Wheat straw	0.05	5	75–83	78	3.2
	0.5	5	78–89	83	3.9
Rape seed	0.05	5	80–90	88	5.8
	0.5	5	87–97	93	3.8
Orange fruit	0.05	5	69–81	74	5
	0.5	5	73–86	81	6
Melon fruit	0.05	5	82–93	85	5
	0.5	5	82–95	89	5

Tea

An independent laboratory method validation was conducted by Marin, (2008, 2008/1042807) to determine the validity of the procedure P 1340G to analyse flufenoxuron in tea (green).

Table 28 Independent laboratory recovery results of method P 1340G

Matrix	No. of tests	Fortification level [mg/kg]	Transition (m/z= 489 → 158) [a]			Transition (m/z= 489 → 141)		
			Range of Recoveries[%]	mean [%]	SD [+/–]	Range of Recoveries [%]	mean [%]	SD [+/–]
Tea (green)	5	0.1	65–81	75	7	63–80	72	7
	5	10	76–88	80	5	73–85	78	4

[a] Used for quantitation

Animal materials

Method SAMS 486-1 involves treating a sample of milk with potassium oxalate solution and ethanol followed by extraction with diethyl ether and hexane. The diethyl ether is removed by evaporation and the hexane is partitioned with acetonitrile. The acetonitrile is exchanged for a mixture of hexane, ethanol and acetic acid and cleaned-up by normal phase HPLC. Residues of flufenoxuron are determined by reverse-phase HPLC with UV detection at 254 nm.

The applicability of the method was confirmed by an independent laboratory by Skorczynski (1997, RES 97-027) where parent flufenoxuron was analysed with a validated LOQ of 0.01 mg/kg (Table 29).

Table 29 Independent laboratory recovery results of method SAMS 486-1

Matrix	Fortification level [mg/kg]	No. of tests	Range of Recoveries [%]	Mean Recovery [%]
Milk	0.01	2	84–85	85
	0.02	2	89–110	100

Method SAMS 458-1, involves extracting residues of flufenoxuron in fat with methylene chloride and sodium sulphate, followed by evaporation to dryness, then re-dissolving the residue in hexane followed by solid-phase extraction clean-up and reversed-phase HPLC-clean-up. Determination of residues of flufenoxuron is performed by normal-phase HPLC with UV-detection at 254 nm.

The applicability of the method was confirmed in an independent laboratory by Skorczynski (1997, RES 97-037) where parent flufenoxuron was analysed with a validated LOQ of 0.05 mg/kg (Table 30).

Table 30 Independent laboratory recovery results of method SAMS 458-1

Matrix	Fortification level [mg/kg]	No. of tests	Range of Recoveries[%]	Mean Recovery [%]
Beef fat	0.05	2	75–93	84
	0.1	2	77–81	79

STABILITY OF PESTICIDES IN STORED SAMPLES

Plant materials

The storage stability of flufenoxuron has been investigated in various plant matrices for a storage period of up to 36 months.

The storage stability of flufenoxuron was investigated in cottonseed, orange, grape and apple for up to 36 months (Gillard, D.F., 1993a, FX-326-004), in lettuce for 27 months (Edwards, 2000?a, 2000/1021958; Farell, 1996a, FX-726-003) and in watermelon peel and pulp for 25–26 months (Edwards, 2000b, 2000/1021961; Edwards, 2000c, 2000/1021962).

Homogenised samples were weighed into glass jars and fortified individually at levels of 0.1 mg/kg (cottonseed, orange, grape and apple) and 0.5 mg/kg (lettuce, watermelon peel and pulp). After fortification, the solvent was allowed to evaporate. In addition, untreated samples of each sample material were prepared for control and recovery experiments. Subsequently the jars were closed and stored deep frozen until analysis (except for the day 0 samples). At each sampling interval, 2–3 fortified and two control samples were removed from the deep-freezer. Subsequently, one of the control samples of each sample material was freshly fortified with flufenoxuron to determine the concurrent recoveries. Fortification levels were at the same magnitude as the spiked storage samples.

The grape and apple samples were analysed according to the Analytical Method SAMS 423-3. Briefly, flufenoxuron is extracted from the samples by blending with methylene chloride and sodium sulfate. An aliquot of the extract was concentrated to dryness and cleaned up by solid phase extraction prior to HPLC analysis.

The cottonseed and orange samples were analysed according to the Analytical Method SAMS 454-1 where flufenoxuron was extracted by blending with acetone:hexane (v:v) and sodium sulphate. An aliquot of the extract was concentrated to dryness, reconstituted in acetonitrile and partitioned with hexane. The acetonitrile phase was cleaned up by solid phase extraction prior to HPLC analysis.

Lettuce samples were analysed using Analytical Method RLA 12466.00V while watermelon peel and pulp samples were analysed using Analytical Method RLA 12482.00V. No description was provided of either method.

No significant degradation of the flufenoxuron residues was observed in cottonseed, orange, grape and apple up to 36 months of storage, in lettuce for 27 months and watermelon (pulp and peel) for up to 26 months (Table 31).

Table 31 Storage stability of flufenoxuron in plant commodities fortified with flufenoxuron at 0.1 mg/kg

Matrix	Storage Period (months)	Residue levels in stored samples [a] (%)			Procedural recoveries [a] (%)
		Individual Values	Mean	RSD (%)	Individual Values
Cottonseed	0	126.0, 125.8, 132.0	128	2.8	125.2
	3	107.8, 87.0	98	–	97.4
	6	92.0, 95.0, 81.0	89	8.2	80.0
	12	123.2, 113.2, 130.0	122	6.9	126.4
	14	–	–	–	–
	18	100.8, 104.0, 113.5	106	6.2	121.2
	24	91.2, 104.4, 86.8	94	9.7	110.4
	36	84.2, 79.8, 77.0	80	4.5	81.0
Orange	0	93.2, 112.0, 111.2	105	10.1	116.8
	4	102.8, 114.8, 110.4	109	5.6	119.6
	6	113.2, 113.2, 118.4	115	2.6	116.0
	12	–	–	–	–
	14	126.8, 105.6	117	–	112.8
	18	106.0, 115.4, 120.0	114	6.3	106.6
	24	95.0, 90.8, 84.8	91	5.7	89.6
	36	85.2, 97.2, 87.6	90	7.1	97.6
Grape	0	109.0, 114.0, 109.0	111	2.6	115.0
	3	120.0, 128.5, 106.5	119	9.4	107.0
	6	105.0, 107.0, 106.0	106	0.9	101.0
	12	–	–	–	–
	14	110.0, 109.5	110	–	128.5
	18	119.5, 127.0, 127.0	125	3.5	127.5
	24	116.0, 118.5, 128.5	121	5.5	94.5
	36	81.5, 93.0, 111.0	95	15.6	89.5
Apple	0	105.5, 98.5	103	–	101.5
	3	119.5, 115.0	118	–	98.0
	6	104.0, 106.5, 121.0	111	8.3	95.5
	12	–	–	–	–
	14	114.0, 124.0	119	–	121.0
	18	129.0, 123.5, 127.5	126	2.2	111.0
	24	79.0, 98.0, 104.5	94	14.1	88.5
	36	110.8, 109.4, 105.8	109	2.4	103.5
Lettuce	0	108, 107	108	–	110
	1	94, 93	94	–	106
	3	74, 96	85	–	98

Matrix	Storage Period (months)	Residue levels in stored samples [a] (%)			Procedural recoveries [a] (%)
		Individual Values	Mean	RSD (%)	Individual Values
	14	89, 85	87	–	104
	18	96, 87	92	–	88
	27	87, 85	86	–	90
Watermelon peel	0	108, 107	108	–	107
	1	101, 92	97	–	107
	3	88, 85	87	–	92
	14	106, 102	104	–	109
	18	83, 85	84	–	89
	26	69, 80	75	–	101
Watermelon pulp	0	109, 108	109	–	109
	1	104, 102	103	–	110
	3	105, 97	101	–	109
	14	99, 97	98	–	98
	18	88, 89	89	–	95
	26	79, 92	86	–	78

[a] Reported as a function of the nominal (0.1 mg/kg) spiking level

Animal Materials

For animal matrices, the storage stability of flufenoxuron has been investigated for a storage period of up to 12 months (Lewis 1993a, FX-326-003).

The freezer stability of flufenoxuron in various animal matrices was investigated over a period of one year (53 weeks). Untreated bovine muscle, liver, kidney, fat and milk and hen skin, egg yolk and egg white samples were fortified with radiolabelled flufenoxuron at three different concentrations. The samples were stored at -19 °C. All beef and hen skin samples were analysed according to the Analytical Method SAMS 457-2 with a slight modification for extracting heparin-treated blood. Egg yolk and egg white samples were analysed according to the Analytical Method SAMS 492-1. Cow's milk samples were analysed based on the Analytical Method SAMS 486-1. Residues were analysed by TLC, HPLC-UV and LSC.

No significant degradation of the flufenoxuron residues was observed in any of the animal matrices except egg whites where a steady decline was noted by 53 weeks (31% dissipation).

Table 32 Storage stability of flufenoxuron in animal commodities

Commodity	Fortification Level (mg/kg)	Recoveries in stored samples [a] (%) Duration (weeks)				
		0	4	13	26	53
Bovine muscle	0.107	83	61	67	62	61
	1.09	84	62	72	63	66
	11.3	83	63	67	63	68
Bovine liver	0.108	87	75	79	76	84
	1.08	83	73	71	79	88
	10.9	89	75	85	83	87
Bovine kidney	0.108	88	79		70	77
	1.10	89	73	–	76	78
	11.3	88	72		77	81
Bovine fat	0.106	98	103	92	94	92
	1.04	98	104	95	99	90
	10.9	97	102	92	94	91
Cow's milk	0.0556	88	86	85	90	87
	0.56	91	90	80	78	89
	5.91	88	88	84	84	86
Bovine blood	0.0547	82	80	67	68	83
	0.578	79	77	68	65	84
	5.94	79	81	72	71	84

Commodity	Fortification Level (mg/kg)	Recoveries in stored samples [a] (%) Duration (weeks)				
		0	4	13	26	53
Hen skin	0.109	97	95		85	92
	1.11	96	92	–	80	90
	11.5	96	90		89	89
Egg yolk	0.109	95	94		83	89
	1.09	92	94	–	89	87
	11.8	89	87		81	82
Egg white	0.110	96	NA	62	70	65
	1.14	93	81	63	80	64
	11.6	94	82	71	66	76

[a] Reported as total percent applied radioactivity, are a function of the specified fortification level.

USE PATTERN

Flufenoxuron is a new benzoylurea type of acaricide/insecticide which inhibits chitin biosynthesis in nymphal mites and caterpillars. Flufenoxuron is registered in Brazil and in Japan as an emulsifiable concentrate (EC).

The Meeting received the registered label from Brazil for orange, apple and from Japan for tea in the original languages as well as the English translations.

Table 33 List of uses of flufenoxuron

Crop	Country	Application			Application rate per treatment			PHI [days]
		Method	No. per season	Application interval [days]	kg ai/hL	Water L/ha	kg ai/ha	
Orange	Brazil	spray	2	30	0.003–0.005	–	–	15
Apple	Brazil	spray	–	–	0.01	1200–2000		35
Tea	Japan	spray	2	7–14	0.0025	2000–4000	0.05–0.1	7

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

Residue levels were reported as measured. Application rates were always reported as flufenoxuron equivalents. When residues were not quantifiable they are shown as below the LOQ, e.g., < 0.01 mg/kg.

Application rates and spray concentrations have generally been rounded to two significant figures.

All samples were analysed using either an HPLC-UV method (254 nm) which involved extraction with DCM and sodium sulphate and a validated LOQ of 0.05 mg/kg or an HPLC/MS/MS method involving extraction with methanol/water/HCl and partitioning in water cyclohexane with an LOQ of 0.01 mg/kg.

Laboratory reports included method validation including batch recoveries at fortification levels bracketing the LOQ, 10× LOQ and 100× LOQ. Dates of analyses or duration of residue sample storage were also provided. These storage intervals were covered by the storage stability studies on parent in high oil, high acid and high water content matrices.

Field reports provided data on the sprayers used and their calibration, plot size, residue sample size and sampling date. Although trials included control plots, no control data are recorded in the tables as residues in control samples were below the method LOQ. Residue data are recorded unadjusted for % recovery. Where multiple samples were taken from a single plot or where multiple analyses were conducted for the same sample, the average value is reported, with the individual

values captured in brackets. Residues from trials conducted according to critical GAP are underlined and have been used for the estimation of maximum residue levels, STMR and HR values.

Crop	Field/Greenhouse	Treatment Type	Countries	Table
Orange	Field	Foliar spray	Brazil, Greece, Italy, South Africa	34
Apple	Field	Foliar spray	Chile	35
Tea	Field	Foliar spray	Japan	36

Oranges

Eleven supervised residue trials were conducted during 1986, 2007 and 2011 on oranges grown in Brazil and treated once or twice with a soluble concentrate (SL) or dispersible concentrate (DC) formulation of flufenoxuron at rates of 0.003–0.005 kg ai/hL. Oranges were harvested 0–28 days following the last application. In the 1986 trials, residues are reported in peel and pulp based on ratios of 37% peel and 63%pulp. For the remaining trials, the residues are reported on a whole fruit basis.

Five additional orange trials, involving application of a DC formulation, were also conducted in Greece (two; 1996), Italy (one, 1996) and South Africa (two; 1989). The number of applications and treatment rates for Greece, Italy and South Africa were 2× 0.005 kg ai/hL, 2× 0.008 kg ai/hL and 1× 0.005 kg ai/hL, respectively. Oranges were harvested 0–28 days following the last application and separated into peel and pulp prior to analysis.

Table 34 Residues of flufenoxuron in oranges following foliar spray with SL or DC formulations

Trial location, Country, Year (Variety)	Application					Growth Stage	DAT, days	Matrix	Flufenoxuron Residues [a] (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	no.	RTI, days					
cGap Brazil	100 g/L		0.003–0.005	2	30		15			
Mogi-Mirim-SP, Brazil, 1986 (Pera Coroa)	SL 50 g/L	0.04	0.003	1	NA	Ripening	3 3 3 7 7 7 15 15 15	Peel Pulp Whole fruit [b] Peel Pulp Whole fruit [b] Peel Pulp Whole fruit [b]	0.11 < 0.02 0.05 0.05 < 0.02 0.03 0.06 < 0.02 0.03	I/BER/RE/CI-01185
Mogi-Mirim-SP, Brazil, 1986 (Pera Coroa)	SL 50 g/L	0.04	0.005	1	NA	Ripening	3 3 3 7 7 7 15 15 15	Peel Pulp Whole fruit [b] Peel Pulp Whole fruit [b] Peel Pulp Whole fruit [b]	0.2 < 0.02 0.09 0.2 < 0.02 0.09 0.2 < 0.02 0.09	I/BER/RE/CI-01185
Palea Korinthos, Greece, 1996 (Navalline)	DC	0.08–0.11	0.005	2	151	BBCH 85–89	14 14 14 28 28 28	Peel Pulp Whole fruit [c] Peel Pulp	0.23 < 0.05 0.11 0.27 < 0.05 0.13	96-651-01

Trial location, Country, Year (Variety)	Application					Growth Stage	DAT, days	Matrix	Flufenoxuron Residues [a] (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	no.	RTI, days					
								Whole fruit[2)]		
Drosia Chalkidas,, Greece, 1996 (Navalline)	DC	0.07–0.11	0.005	2	153	BBCH 85–89	14 14 14 28 28 28	Peel Pulp Whole fruit [c] Peel Pulp Whole fruit [c]	0.61 < 0.05 0.25 0.43 < 0.05 0.31	96-651-02
Castellanita Marina, Italy, 1996 (Navalin)	DC 50 g/L	0.07	0.008	2	14	BBCH 85–87	0 0 0	Peel Pulp Whole fruit [b]	0.33 < 0.05 0.15	96-556-01
							7 7 7	Peel Pulp Whole fruit [b]	0.36 < 0.05 0.16	
							14 14 14	Peel Pulp Whole fruit [b]	0.28 < 0.05 0.14	
							21 21 21	Peel Pulp Whole fruit [b]	0.31 < 0.05 0.15	
							28 28 28	Peel Pulp Whole fruit [c]	0.16 < 0.05 0.09	
South Africa, 1989 (Navel)	DC	NS	0.003	1	NA	Ripening	0 0 0 7 7 7 13 13 13 28 28 28	Peel Pulp Whole fruit [c] Peel Pulp Whole fruit [c] Peel Pulp Whole fruit [c] Peel Pulp Whole fruit [c]	0.26 0.01 0.04 0.24 < 0.01 0.07 0.45 < 0.01 0.10 0.33 < 0.01 0.08	FX-710-005
South Africa, 1989 (Navel)	DC	NS	0.005	1	NA	Ripening	0 0 0 7 7 7 13 13 13 28 28 28	Peel Pulp Whole fruit [c] Peel Pulp Whole fruit [c] Peel Pulp Whole fruit [c] Peel Pulp Whole	0.43 0.01 0.13 0.51 < 0.01 0.15 0.46 < 0.01 0.09 0.48 < 0.01 0.12	FX-710-005

Trial location, Country, Year (Variety)	Application					Growth Stage	DAT, days	Matrix	Flufenoxuron Residues [a] (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	no.	RTI, days					
								fruit [c]		
Santo Antonio de Posse, Brazil, 2007 (Pera)	DC	0.06	0.003	2	NS	BBCH 88	0 5 10 15 20	Whole fruit	0.05 (0.05, 0.05) 0.06 (0.06, 0.06) 0.05 (0.04, 0.05) 0.07 (0.05, 0.04 0.09, 0.07) 0.06 (0.05, 0.06)	EC-CD-BRUA/1100-06
Uberlandia, Brazil, 2007 (Natal)	DC	0.06	0.003	2	NS	BBCH 83	0 6 10 15 20	Whole fruit	0.12 (0.11, 0.12) 0.10 (0.10, 0.10) 0.11 (0.10, 0.11) 0.10 (0.09, 0.10) 0.07 (0.07, 0.06)	EC-CD-BRVA/1100-06
Pirassununga, Brazil, 2007 (Valência)	DC	0.06	0.003	2	NS	BBCH 87	15	Whole fruit	0.05 (0.05, 0.04)	EC-R-BRUB/1100-06
Estiva Gerbi, Brazil, 2007 (Valência)	DC	0.06	0.003	2	NS	BBCH 88	15	Whole fruit	0.08 (0.09, 0.06)	EC-R-BRUC/1100-06
Santo Antonio de Posse, Brazil, 2011 (Natal)	DC	0.10	0.005	2	30 [d]	BBCH 87	0 7 15 21	Whole fruit	0.13 (0.16, 0.13, 0.12, 0.12) 0.14 (0.18, 0.14, 0.13, 0.13) <u>0.13</u> (0.13, 0.13, 0.13, 0.12) 0.12 (0.15, 0.10, 0.10, 0.11)	G100555
Sao Sebastiao, da Amoreira, Brazil, 2011 (Navelina)	DC	0.10	0.005	2	30 [d]	BBCH 81	15	Whole fruit	<u>0.09</u>	G100557
Tamarana, Brazil, 2011 (Folha murcha)	DC	0.10	0.005	2	30 [d]	BBCH 85	15	Whole fruit	<u>0.16</u> (0.20, 0.14, 0.14, 0.15)	G100631
Jaboticabal, Brazil, 2011 (Pera)	DC	0.08	0.002	2	30 [d]	BBCH 83	0 7 15 20	Whole fruit	0.05 0.02 0.03 < 0.01	G100697
Jaboticabal, Brazil, 2011 (Pera)	DC	0.10	0.005	2	30 [d]	BBCH 81	0 7 15 21	Whole fruit	0.13 0.10 <u>0.11</u> 0.10	G100737

SL: Soluble concentrate
DC: Dispersible concentrate
[a] When there are 2 residues per PHI, the replicate samples from the same plot where there are 4 residues per PHI, these represent four replicate samples from two plots.

[b] Calculated using a ratio of 37% peel and 63% pulp
[c] Calculated using the exact peel and pulp samples
[d] Determined based on dates of application

Apples

Fourteen supervised residue trials were conducted in Chile during the 1988–1990 growing seasons on apples treated once, early season, with flufenoxuron at rates of 0.01–0.02 kg ai/hL and harvested 35–150 days following application.

Table 35 Residues of flufenoxuron in apples following foliar spray

Trial location, Country, Year (Variety)	Application					Growth Stage	DAT, days	Flufenoxuron Residues (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.				
cGap Brazil	100 g/L		0.01	1200–2000	1		35		
San Fernando, Chile, 1988 (variety not specified)	NS	0.22	0.01	2200	1	prior to bloom	35	0.45	UCH-SF
							77	< 0.05	
							113	< 0.05	
							126	< 0.05	
	NS	0.33	0.015	2200	1	prior to bloom	35	0.52	
							77	< 0.05	
							113	< 0.05	
							126	< 0.05	
	NS	0.44	0.02	2200	1	prior to bloom	35	0.43	
							77	0.08	
							113	< 0.05	
							126	< 0.05	
Requinoa, Chile, 1988 (variety not specified)	NS	0.18	0.01	1800	1	10–15 mm diameter fruit	15	0.28	UCH-R
							36	0.07	
							49	< 0.05	
							85	< 0.05	
							98	< 0.05	
	NS	0.36	0.02	1800	1	10–15 mm diameter fruit	15	0.46	
							36	0.17	
							49	0.09	
							85	0.12	
							98	0.05	
Teno, Chile, 1988 (Red King Oregon)	NS	0.16	0.01	1560	1	Pink bud	150	< 0.05	CHA 187001
		0.23	0.02				150	< 0.05	
		0.31	0.02				150	< 0.05	
Chimbarongo-Rosselot, Chile, 1988 (Granny-spur)	NS	0.35	0.01	3500	1	90% bloom	148	< 0.05	CHA 187002
		0.52	0.02				148	< 0.05	
		0.70	0.02				148	< 0.05	
Chimbarongo-Donoso, Chile, 1988 (Red King Oregon)	NS	0.86 & 0.64	0.02 & 0.015	4280	2	Pink bud 7–8mm fruit	127	< 0.05	CHA 187003
Chimbarongo-Donoso, Chile, 1988 (Granny-spur)	NS	0.44	0.01		1			< 0.05	
		0.64	0.02			50% bloom	146	< 0.05	
		0.86	0.02					< 0.05	
Olivar-Alto, Chile, 1988 (Red-spur)	NS	0.32	0.01	3180	1	Pink bud 10% bloom	145	< 0.05	CHA 187004
		0.48	0.02				145	< 0.05	
		0.64	0.02				145	< 0.05	
Pelequen, Chile, 1988	NS	0.59	0.02	3950	1	8 mm fruit	125	< 0.05	CHA 187005
		0.40	0.01			95% bloom	141	< 0.05	

Trial location, Country, Year (Variety)	Application					Growth Stage	DAT, days	Flufenoxuron Residues (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.				
(Red King Oregon)		0.59	0.02			95% bloom	141	< 0.05	
		0.79	0.02			95% bloom	141	< 0.05	
Molina, Chile, 1988 (Red King Oregon)	NS	0.16	0.01	1650	1			< 0.05	CHA 187006
		0.25	0.02			80% bloom	139	< 0.05	
		0.33	0.02					< 0.05	
Curico, Chile, 1988 (Granny spur)	NS	0.57	0.01	5680	1	100% petal	138	< 0.05	CHA 187007
Curico Chile, 1988 (Richared)	NS	0.85	0.02	5680	1	50% petal	138	< 0.05	
		1.14	0.02					< 0.05	
Rosario, Chile, 1988 (Richared Delicious)	NS	0.44	0.01	4360	1			< 0.05	CHA 187008
		0.65	0.02			Fruit set 2 mm fruit	133	< 0.05	
		0.87	0.02					< 0.05	
Tinguiririca, Chile, 1988 (Red King Oregon & Red Dpur)	NS	0.77	0.01	5140	1	Fruit set	131	< 0.05	CHA 187009
		1.03	0.02					< 0.05	
Requinoa, Chile, 1990 (Red Spur)	DC 100 g/L	0.42	0.05	8320	1	Developing fruit 10 mm	6	0.24	FX-711-028
							20	0.07	
							41	0.04	
							55	0.02	
							harvest	<0< 0.01	
	DC 100 g/L	0.62	0.08	8320	1	Developing fruit 10 mm	6	0.32	
							20	0.23	
							41	0.16	
							55	0.03	
							harvest	<0< 0.01	

NS: Not specified

Pears

Two trials were conducted on a same site located in Chile, during the 1990 growing season, on pears treated once early season with a DC formulation at rates of 0.2–0.38 kg ai/ha and harvested 0–60 days following application.

Table 36 Residue decline of Flufenoxuron in pears following foliar spray with DC Formulation

Trial location, Country, Year (Variety)	Application					Growth Stage	DAT, days	Flufenoxuron Residues (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.				
Requinoa, Chile, 1990 (Red Spur)	DC 100 g/L	0.2	NS	NS	1	Developing fruit	0 6 20 27 41 60	1.0 0.45 0.3 0.13 0.03 < 0.01	FX-711-028
	DC 100 g/L	0.38	NS	NS	1	Developing fruit	0 6 20 27 41 60	2.62 0.82 0.42 0.30 0.07 0.03	

NS: Not specified

Melons

Melons, grown in Brazil during the 2010 season, received four applications of a DC formulation of flufenoxuron at 0.01 kg ai/hL, with 4–7 day re-treatment intervals, and harvested 0–10 days following the last application. For some trials, residues in pulp and peel were determined from whole fruit, based on a ratio of 40% peel and 60% pulp.

Table 37 Residues of flufenoxuron in field grown melons following foliar spray with DC formulation

Location, year (Variety)	Application						Growth Stage	DAT, days	Matrix	Flufenoxuron Residues (mg/kg) [b]	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.	RTI, days					
Ponta Grossa, Brazil, 2010 (Redondo Gaucho)	DC 100 g/L	0.10	0.01	1000	4	4	89	10	Whole Fruit	0.07	G080414
Assai, Brazil, 2010 (Hibrido Louis)	DC 100 g/L	0.10	0.01	1000	4	4	77	10	Whole Fruit	0.03	G080415
Mossoro, Brazil, 2010 (Galia)	DC 100 g/L	0.10	0.01	1000	4	4	81	10	Whole Fruit	0.03	G080416
Anhembi, Brazil, 2010 (Casca de Carvalho)	DC 100 g/L	0.10	0.014	700	4	NS	83	0	Peel	0.20	EC-CD-BRUA/1099-06
								0	Pulp	0.08	
								0	Whole Fruit [a]	0.13	
								1	Peel	0.16	
								1	Pulp	0.06	
								1	Whole Fruit [a]	0.10	
								3	Peel	0.17	
								3	Pulp	0.08	
								3	Whole Fruit [a]	0.12	
								5	Peel	0.15	
								5	Pulp	0.03	
								5	Whole Fruit [a]	0.08	
								7	Peel	0.08	
								7	Pulp	< 0.01	
								7	Whole Fruit [a]	0.04	
								10	Peel	0.10	
								10	Pulp	< 0.01	
								10	Whole Fruit [a]	0.05	
Icapui, Brazil, 2010 (Amarelo Gold Mine)	DC 100 g/L	0.10	0.014	700	4	NS	80	0	Peel	0.16	EC-CD-BRUC/1099-06
								0	Pulp	0.01	
								0	Whole Fruit [a]	0.07	
								1	Peel	0.14	
								1	Pulp	0.01	
								1	Whole Fruit [a]	0.06	
								3	Peel	0.09	

Location, year (Variety)	Application						Growth Stage	DAT, days	Matrix	Flufenoxuron Residues (mg/kg) [b]	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.	RTI, days					
								3	Pulp	0.01	
								3	Whole Fruit [a]	0.04	
								5	Peel	0.07	
								5	Pulp	< 0.01	
								5	Whole Fruit [a]	0.03	
								7	Peel	0.17	
								7	Pulp	< 0.01	
								7	Whole Fruit [a]	0.07	
								10	Peel	0.1	
								10	Pulp	0.02	
								10	Whole Fruit [a]	0.05	
Anhembi, Brazil, 2010 (Casca de Carvalho)	DC 100 g/L	0.10	0.014	700	4	NS	83	3	Peel	0.17	EC-R-BRUA/1099-06
								3	Pulp	0.01	
								3	Whole Fruit [a]	0.07	
								7	Peel	0.09	
								7	Pulp	< 0.01	
								7	Whole Fruit [a]	0.04	
Mossoro, Brazil, 2010 (Amarelo Gold Mine)	DC 100 g/L	0.10	0.014	700	4	NS	80	3	Peel	0.14	EC-R-BRUB/1099-06
								3	Pulp	< 0.01	
								3	Whole Fruit [a]	0.06	
								7	Peel	0.1	
								7	Pulp	< 0.01	
								7	Whole Fruit [a]	0.05	
Anhembi, Brazil, 2010 (Imperial)	DC 100 g/L	0.10	0.014	700	4	NS	84	3	Peel	0.19	EC-R-BRUB/11099-06
								3	Pulp	0.18	
								3	Whole Fruit [a]	0.18	
								7	Peel	0.11	
								7	Pulp	< 0.01	
								7	Whole Fruit [a]	0.05	
Lodrina, Brazil, 2010 (Lovis)	DC 100 g/L	0.10	NS	NS	4	4	85	0	Peel	0.46	G100218
									Pulp	< 0.01	
									Whole Fruit	0.12	
							79	3	Peel	0.54	
									Pulp	< 0.01	
									Whole Fruit	0.09	
							75	7	Peel	0.33	

Location, year (Variety)	Application						Growth Stage	DAT, days	Matrix	Flufenoxuron Residues (mg/kg) [b]	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.	RTI, days					
									Pulp	< 0.01	
									Whole Fruit	0.07	
Ibipora, Brazil, 2010 (Lovis)	DC 100 g/L	0.10	NS	NS	4	4	61	0	Peel	0.73	G100219
									Pulp	< 0.01	
									Whole Fruit	0.2	
							57	3	Peel	0.27	
									Pulp	< 0.01	
									Whole Fruit	0.08	
							51	7	Peel	0.28	
									Pulp	< 0.01	
									Whole Fruit	0.08	
Senador Canedo, Brazil, 2010 (Gaúcho)	DC 100 g/L	0.10			4	4	87	3	Peel	0.55	G100220
									Pulp	0.02	
									Whole Fruit	0.21	
Mossoro, Brazil, 2010 (Goldex)	DC 100 g/L	0.10			4	4	79	3	Peel	0.29	G100221
									Pulp	< 0.01	
									Whole Fruit	0.06	

NS: Not specified
[a] Calculated assuming a weight ratio of 40% peel and 60% pulp
[b] Residues < LOQ were assumed to be at 0.01 mg/kg

Tomato

Tomatoes, grown in Spain during the 2008 season and maintained under protective cover, were treated twice with a DC formulation of flufenoxuron at 0.12–0.13 kg ai/ha and 14 day re-treatment interval. Mature tomatoes were harvested 0–7 days following the last application.

During the 2008 season, field tomatoes grown in Brazil were treated with four applications of a DC formulation of flufenoxuron at 0.01 kg ai/hL and a 7-day re-treatment interval. Tomatoes were harvested 0–7 days following the last application.

Table 38 Residues of flufenoxuron in tomatoes following spray with DC formulation

Trial location, Country, Year (Variety)	Application						Growth Stage	DAT, days	Flufenoxuron Residues (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.	RTI, days				
Conil de la Frontera, Spain, 2008 (Caramba) Protected	DC 100 g/L	0.12–0.13	0.01	1180–1271	2	14	84 85– 86	0	0.067	AF/12238/PM/1
								3	0.093	
								5	0.084	
								7	0.089	
Conil de la Frontera, Spain, 2008 (Bond)	DC 100 g/L	0.13	0.01	1282–1288	2	14	64 71	7	0.07	AF/12238/PM/2

Trial location, Country, Year (Variety)	Application						Growth Stage	DAT, days	Flufenoxuron Residues (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.	RTI, days				
Protected										
Los Palacios Y Villafranca, Spain, 2008 (V1) Protected	DC 100 g/L	0.12–0.13	0.01	1215–1340	2	14	72 73	7	0.09	AF/12238/PM/3
Zaragoza, Spain, 2008 (Caramba) Protected	DC 100 g/L	0.12–0.13	0.01	1243–1300	2	14	77 81	0 3 5 7	0.16 0.21 0.32 0.24	AF/12238/PM/4
Santa Engracia, Spain, 2008 (Caramba) Protected	DC 100 g/L	0.12–0.13	0.01	1200–1286	2	14	75 77	7	0.1	AF/12238/PM/5
Remolinos, Spain, 2008 (Caramba) Protected	DC 100 g/L	0.13	0.01	1282–1299	2	14	73 87–89	7	0.23	AF/12238/PM/6
Cambados, Spain, 2008 (Disie) Protected	DC 100 g/L	0.13	0.01	1270–1294	2	14	71 73	7	0.1	AF/12238/PM/7
Paende San Vicente Meis, Spain, 2008 (Caramba) Protected	DC 100 g/L	0.12–0.13	0.01	1230–1298	2	14	71 72	7	0.14	AF/12238/PM/8
Ponta Grossa, Brazil, 2008 (Raissa) Field	DC 100 g/L	0.10	0.01	1000	4	7	80	0 3 5 7 10	0.08 0.08 0.07 0.08 0.06	EC-CD-BRTA/1162-06
Santo Antonio de Posse, Brazil, 2008 (Bonus F1) Filed	DC 100 g/L	0.10	0.01	1000	4	7	85	0 3 5 7 10	0.38 0.37 0.36 0.37 0.21	EC-CD-BRUA/1162-06
Araguari, Brazil, 2008 (Alambra) Field	DC 100 g/L	0.10	0.01	1000	4	7	83	3 7	0.07 0.08	EC-R-BRVA/1162-06
Ipiranga, Brazil, 2008 (Raissa) Field	DC 100 g/L	0.10	0.01	1000	4	7	78	3 7	0.05 0.04	EC-R-BRTB/1162-06
Santo Antonio de Posse, Brazil, 2011 (Italiano	DC 100 g/L	0.10	0.01	1000	4	7	89	3 7	0.18 0.19	G100074

Trial location, Country, Year (Variety) Comprido) Field	Application						Growth Stage	DAT, days	Flufenoxuron Residues (mg/kg)	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.	RTI, days				
Senador Canedo, Brazil, 2011 (Carolina) Field	DC 100 g/L	0.10	0.01	1000	4	7	84	3	0.02	G100075
								7	0.02	

Tea

Eleven trials conducted on tea, grown in Japan during the 2005–2007 growing seasons, were treated twice or five times with an EC formulation of flufenoxuron at a rate of 0.0025 kg ai/hL. The re-treatment intervals were not specified in the study report. Tea leaves were harvested 1–14 days following application. On the day of sampling, tea leaves were processed in accordance with the standard green tea processing procedure and individually tightly sealed in a tea can prior to transportation

Table 39 Residues of flufenoxuron in tea (green) following spray with EC formulation

Trial location, Country, Year (Variety)	Application					Growth Stage [a]	DAT, days	Matrix [c]	Flufenoxuron Residues (mg/kg)	Ref
	Form	g ai/ha	0.0025 kg ai/hL	Water, L/ha	no					
cGAP Japan	EC	50–100	25	2000–4000	2/7–14 day RTI		7			
Kagoshima, Japan, 2005 (Okumidori)	EC (10%)	100	25	4000	2	1.0, 2.5	7	Tea (green)	4.58	217858
Shizuoka, Japan, 2005 (Yabukita)	EC (10%)	100	25	4000	2	0.5–1.5, 2.0–3.0	7	Tea (green)	6.02	
Kyoto, Japan, 2005 (Kanayamidori)	EC (10%)	100	25	4000	2	2.0, 3.0	7	Tea (green)	6.23	
Mie, Japan, 2005 (Sayamakaori)	EC (10%)	100	25	4000	2	1.5, 3.0	7	Tea (green)	11.8	
Fukuoka, Japan, 2005 (Meiryoku)	EC (10%)	100	25	4000	2	1.0–1.5, 2.5–3.0	7	Tea (green)	3.95	
Myazaki, Japan, 2005 (Fuushun)	EC (10%)	100	25	4000	2	2.0, 3.0	7	Tea (green)	2.48	
Shizuoka, Japan, 2005 (Yabukita)	EC (10%)	100	25	4000	2	0.5–1.5, 2.0–3.0	7	Tea (green)	2.37	
Japan, 2007 (Okumidori)	EC (10%)	100	25	4000	5	4.0–5.0 [b]	1	Tea (green)	12	P/B 1340G
						3.0–4.0 [b]	7	Tea (green)	6.4	
						2.0–3.0 [b]	14	Tea (green)	3.1	
Japan, 2007 (Yabukita)	EC (10%)	100	25	4000	5	4.0 [b]	1	Tea (green)	14	
						3.0 [b]	7	Tea (green)	5.9	

Trial location, Country, Year (Variety)	Application					Growth Stage [a]	DAT, days	Matrix [c]	Flufenoxuron Residues (mg/kg)	Ref
	Form	g ai/ha	0.0025 kg ai/hL	Water, L/ha	no					
						1.0 [b]	14	Tea (green)	2.4	
Japan, 2007 (Komakage)	EC (10%)	100	25	4000	5	3.5 [b]	1	Tea (green)	13	
						3.5 [b]	7	Tea (green)	6.1	
						2.0 [b]	14	Tea (green)	1.4	
Japan, 2007 (Yabukita)	EC (10%)	100	25	4000	5	4.0–5.0 [b]	1	Tea (green)	19	
						3.5–4.0 [b]	7	Tea (green)	7.4	
						1.5–2.0 [b]	14	Tea (green)	2.7	

[a] Leaf stage
[b] Leaf stage at last application
[c] On the day harvested, tea leaves were processed in accordance with the standard green tea processing procedure and individually tightly sealed in a tea can prior to transportation

FATE OF RESIDUES IN STORAGE AND PROCESSING

Nature of residue during processing

The hydrolysis of flufenoxuron under processing conditions was investigated by Hassink, J. (2003/1000985). [Difluorobenzamide-ring-U-^{14}C]-flufenoxuron and [fluoroaniline-ring-U-^{14}C]-flufenoxuron were diluted in sterile buffered aqueous solution at a nominal concentration of 1 µg ai/L, which corresponds to approximately 50% of the water solubility (at pH 4). Incubation was done at three representative sets of hydrolysis conditions: 90 °C, pH 4 for 20 minutes (pasteurisation); 100 °C, pH 5 for 60 minutes (baking, brewing and boiling) and 120 °C, pH 6 for 20 minutes (sterilisation).

Parent compound and potential hydrolysis products were identified and quantified by HPLC-UV.

Thin layer chromatography was used for confirmation of the identity of the test item by co-chromatography with the non-labelled reference item. Material balances were established for each set of hydrolysis conditions.

Table 40 Hydrolysis of flufenoxuron under simulated processing conditions

Hydrolysis Conditions	Incubation time (min)	[difluorobenzamide-ring-U-^{14}C]-flufenoxuron		[fluoroaniline-ring-U-^{14}C]-flufenoxuron	
		Analyte	% applied radioactivity	Analyte	% applied radioactivity
Pasteurization: pH 4, 90 ºC	20	Flufenoxuron	90.0	Flufenoxuron	92.7
		Unidentified	2.6		
		Total Recovery	92.6	Total Recovery	92.7
Baking, boiling, brewing procedure (pH 5, 100 °C)	60	Flufenoxuron	66.3	Flufenoxuron	
		Reg. No. 102719	32.0	Reg. No. 4064703 or Reg. No. 241208	4.3
		Unidentified	1.9	Unidentified	2.9
		Total Recovery	104.3	Total Recovery	95.7
Sterilization (pH 6, 120 °C)	20	Flufenoxuron	83.5	Flufenoxuron	62.7
		Reg. No. 102719	7.6	Reg. No. 4064702	3.8
		Reg. No. 206925	9.2	Reg. No. 4064703 or Reg. No. 241208	9.5

		Reg. No. 4964847	3.5	Reg. No. 4964847	9.2
		Unidentified	0.2	Unidentified	2.9
		Total Recovery	105.4	Total Recovery	88.1

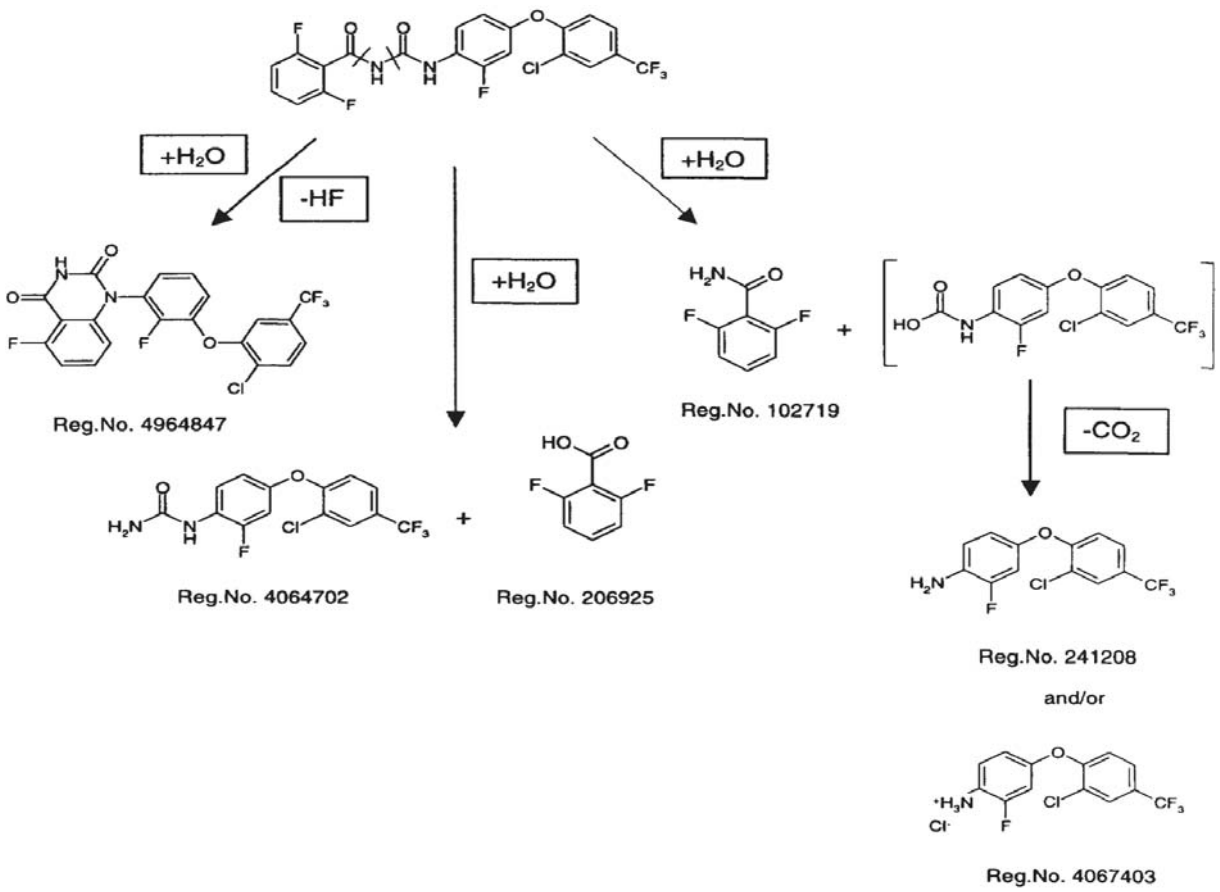


Figure 1 Pathway of hydrolysis of flufenoxuron

Residues after processing

The fate of flufenoxuron during processing of raw agricultural commodity (RAC) was investigated in tomatoes and tea using commercial processing procedures. As a measure of the transfer of residues into processed products, a processing factor (PF) was used, defined as:

$$PF = \frac{\text{Total residue in processed product (mg/kg)}}{\text{Total residue in raw agricultural commodity (mg/kg)}}$$

If residues in the RAC were below the LOQ, no processing factor could be derived. In case of residues below the LOQ, but above the LOD in the processed product, the numeric value of the LOQ was used for the calculation. If residues in the processed product were below the LOD, the numeric value of the LOQ was used for the calculation but the PF was expressed as "less than" (e.g. < 0.5).

A summary of all processing factors for flufenoxuron relevant for the estimation of maximum residue levels of the dietary intake is given in Table 41.

Tomato

Study 1

During the 2002 growing season, four field trials were conducted in field tomatoes in different representative growing areas in southern France and Spain (Smalley R., 2003a; 2003/1004346). The treatment program consisted of three foliar applications of a 100 g/L DC formulation of flufenoxuron at a rate of 0.62 kg ai/ha/application The tomatoes were harvested 6–7 days following the last application, washed and processed according to commercial practices into pomace, juice, sauce and canned tomatoes.

All samples were analysed for flufenoxuron according to method RLA 12675. The limit of quantitation (LOQ) was 0.05 mg/kg.

Samples of processed commodities were stored for up to 600 days prior to analysis of flufenoxuron which is within the demonstrated storage interval for the parent compound in high oil, high acid and high water content matrices.

In the following table, the residues found in processed products are summarised.

Table 41 Residues of flufenoxuron in processed tomato commodities and calculation of processing factors

Location, year, reference (variety)	No.	kg ai/ha	Sample	DAT (days)	Flufenoxuron								
					Residues (mg/kg)				PF [a]				Median PF
S. France and Spain, 2002, 2003/1004346 (Avalon, Ercolé, Perfect Peel, Select Peel)	3	0.62	Tomato	6–7	0.26	1.23	0.41	0.74	–				–
			Tomato before processing		0.14	0.72	0.25	0.51	0.54	0.59	0.61	0.69	0.60
			Washed tomatoes		0.23	0.44	0.29	0.42	0.88	0.36	0.71	0.57	0.63
			Wash water		< 0.05	0.46	n.a.	0.07	0.19	0.37	n.a. [b]	0.09	0.19
			Wet pomace		0.43	0.89	0.43	0.96	1.65	0.72	1.05	1.30	1.18
			Raw juice		0.09	0.49	0.15	0.33	0.35	0.40	0.37	0.45	0.39
			Tomato juice		0.07	0.36	0.13	0.22	0.27	0.29	0.32	0.30	0.30
			Waste puree		1.75	3.53	1.86	2.21	6.73	2.87	4.54	2.99	3.76
			Tomato puree		0.20	0.59	0.23	0.65	0.77	0.48	0.56	0.88	0.67
			Blanching water		< 0.05	< 0.05	< 0.05	< 0.05	0.19	0.04	0.12	0.07	0.10
			Peels		1.54	6.61	1.92	3.52	5.92	5.37	4.68	4.76	5.02
			Peeled tomatoes		< 0.05	< 0.05	< 0.05	< 0.05	0.19	0.04	0.12	0.07	0.10
			Canned tomatoes [c]		< 0.05	0.17	0.05	0.08	0.19	0.14	0.12	0.11	0.13

[a] Processing factor (PF) = residue in processed fraction / residue in RAC
[b] n.a. = sample was not analysed
[c] Raw juice is also added to peeled tomatoes during the process of canning

Study 2

A processing study was conducted in Southern France to determine the residue levels of flufenoxuron and the metabolites Reg. No. 4064702, Reg. No. 102719, Reg. No. 206925, Reg. No. 241208, Reg. No. 4064703 and Reg. No. 4964847 in tomato RAC and processed fractions including canned tomatoes, tomato puree and tomato juice (Ertus, C., 2013; ANADIAG).

The treatment program consisted of a single foliar application of a 100 g/L formulation of flufenoxuron at a rate of 0.5 kg ai/ha made 7 days prior to harvest at the growth stage BBCH 89.

The tomatoes were washed and processed according to the following commercial practices:

For juice production, approximately 8 kg of tomatoes were roughly cut and blended. The mixture obtained was filtered through a fine sieve to separate the juice from peels and seeds. The Brix degree and the pH of the raw juice were determined and the raw juice was heated to 95 °C for 5 minutes. Subsamples of pasteurized juice were stored frozen until analysis.

For production of tomato puree, a juice sample was concentrated under vacuum and gentle heating to 60 °C until reaching a Brix degree of 12. The obtained puree was pasteurized by heating to 95 °C for 5 minutes in a can.

For canning, approximately 2 kg of tomatoes were submerged for about 60 seconds in boiling water and transferred into cold water for 20 seconds to crack the peel. After peeling, subsamples were transferred into glass preserving jars, which were filled up with water, closed and submitted to sterilization. After cooling, canned tomatoes were blended and subsamples were stored frozen until analysis.

All samples were analysed for flufenoxuron and the metabolites according to a method adapted from `Flufenoxuron: Development and Validation of an Analytical Method for Determination and Confirmation of BAS 307I (Flufenoxuron) and its Degradates in Grape—PTRL Europe Study No.P/B1206G`. Briefly, residues were extracted using a mixture of methanol, water and HCl. The centrifuged extract was analysed by LC/MS/MS. The limit of quantification (LOQ) was reported to be 0.01 mg/kg.

Samples of processed commodities were stored for up to 33 days prior to analysis of flufenoxuron and all metabolites which is within the demonstrated storage interval for the parent compound in high oil, high acid and high water content matrices.

In the following table, the residues found in processed products are summarised.

Table 42 Residues of Flufenoxuron and associated metabolites in processed tomato commodities and calculation of processing factors

Location, year, reference (variety)	No.	kg ai/ha	Sample	DAT(days)	Residues (mg/kg)							PF [a]
					Flufenoxuron	Reg. No. 4064702	Reg. No. 102719	Reg. No. 206925	Reg. No. 241208	Reg. No. 464703	Reg. No. 4964847	Flufenoxuron
S. France, 2012, ANADI AG (Rio Grande)	3	0.5	Tomato	6–7	0.28	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	–
			Fresh tomatoes		0.18	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	0.64
			Canned tomatoes		< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	0.04
			Tomato puree		0.08	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	0.28
			Tomato juice		0.04	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	0.14

[a] Only processing factors for flufenoxuron were reported as residues of all other metabolites were not detected above the limit of quantitation (0.01 mg/kg).

Tea

Two residue trials were conducted in 1990 in Kyoto and Kagoshima, Japan (Class, T., 2007a). Flufenoxuron was applied either once or twice at a rate of 0.0025 kg ai/hL and leaves were harvested 7–14 days following application.

An infusion was prepared from the treated dried green tea leaves by adding 360 mL boiling water to 6 g tea and leaving to stand for five minutes.

Dried tea (green) leaves and tea infusion were analysed using the HPLC-UV method titled Pesticide Residue Analysis for Crop (Shell Corporation, 1996). In summary, the method involves extracting flufenoxuron residues with acetone, in the presence of zinc acetate. The filtrates were extracted with ethyl acetate and subjected to hexane/acetonitrile partition after which the acetonitrile phase is purified using a florisil cartridge prior to HPLC–UV analysis. The limit of quantitation for both tea leaves and tea infusion was reported as 0.02 mg/kg, each.

Samples of tea leaves and tea infusion were stored for up to 108 days prior to analysis of flufenoxuron which is within the demonstrated storage interval for parent in high oil, high acid and high water content matrices.

Table 43 Determination of transfer of residues from treated dried tea (green) leaves to tea infusion

	Treatment times	DAT [a]	Residues in dried tea (green)leaves (mg/kg)		Residues in tea infusion (mg/kg)		% transfer from dried tea (green) leaves to tea infusion
			Found	Mean	Found	Mean	
Kyoto	1	7	6.66, 6.26	6.46	0.04, 0.04	0.04	0.62
	1	14	5.57, 5.18	5.36	0.03, 0.03	0.03	0.56
	2	7	7.98, 7.89	7.94	0.06, 0.05	0.06	0.76
	2	14	6.33, 5.96	6.14	0.04, 0.03	0.04	0.65
Kagoshima	1	7	7.75, 7.57	7.65	0.05, 0.05	0.05	0.65
	1	14	4.09, 4.08	4.08	0.03, 0.03	0.03	0.74
	2	7	7.24, 7.19	7.22	0.05, 0.05	0.05	0.69
	2	14	3.63, 3.53	3.58	0.02, 0.02	0.02	0.56
Median transfer							0.65

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

For the estimation of residues of flufenoxuron in animal matrices lactating cow and laying hen feeding studies were submitted to the Meeting.

Lactating dairy cattle

Residues of flufenoxuron in lactating cows were investigated by Gilland Pack (1993). Flufenoxuron was administered orally to fifteen lactating Friesian dairy cows (three cows/control and treatment group and a depuration group consisting of three cows), between 4–7 years of age and in the weight range of 466–602 kg, for 90 consecutive days. Based on a feeding rate of approximately 20 kg/day, dose levels were 1.75, 5.25 and 17.5 mg/kg feed corresponding to 0.07, 0.21 and 0.7 mg/kg bw/day. Animals were dosed twice daily at half of the daily rate at each milking. The average daily milk production ranged from 13–21 kg starting 14 days prior to dosing up to the last day of dosing. The fat content of milk samples taken on days 7, 28, 56 and 90 of the study ranged from 2.5–4.3%.

Milk was collected twice daily. At the end of the dosing period, two composite milk samples were taken for processing to pasteurized milk, cream, skimmed milk and acid whey.

Three animals from the highest dose level group and one control animal were monitored for flufenoxuron residues over a 40-day depuration phase. Milk from these animals was sampled during the depuration period.

Approximately one day after the last day of dosing, the animals, with the exception of the cows of the depuration group, were sacrificed and liver, kidney, composite muscle (pectoralis/adductor muscle of thigh) and perirenal fat (perirenal/omental) were collected for analysis.

Analysis of the samples of milk and milk products was performed using the Analytical Method SAMS 486-1 with minor modifications. The limit of quantitation of this method for flufenoxuron in milk and milk products was reported to be 0.001 mg/L based on acceptable concurrent recoveries. Analysis of the bovine tissues was carried out in duplicate according to a slightly modified version of the Analytical Method SAMS 457-2. The lowest limit of method validation for flufenoxuron in animal tissues is 0.10 mg/kg for muscle, liver and kidney and 0.30 mg/kg for fat based on acceptable concurrent recoveries.

Residues of flufenoxuron in milk are presented in the following table:

Table 44 Residues of Flufenoxuron in milk after administration of Flufenoxuron at 1.75, 5.25 or 17.5 mg/kg feed/day

Study Day	Mean residues for flufenoxuron (mg/L)			
	Group A [a] control	Group B [a] 1.75 mg/kg diet	Group C [a] 5.25 mg/kg diet	Group D [b] 17.5 mg/kg diet
–3	< 0.001	< 0.001	< 0.001	< 0.001
–1	< 0.001	< 0.001	< 0.001	< 0.001
1	< 0.001	< 0.001	< 0.001	0.003 ((0.003, 0.002, 0.003, 0.003, 0.005, 0.002)
2	< 0.001	0.02 (0.025, 0.023, 0.025)	0.07 (0.059, 0.077, 0.068)	0.21 ((0.099, 0.12, 0.25, 0.35, 0.29, 0.13)
4	< 0.001	0.08 (0.091, 0.075, 0.084)	0.21 0.27, 0.24, 0.13)	0.71 (0.73, 0.66, 0.75, 0.87, 0.83. 0.41)
7	< 0.001	0.13 (0.11, 0.12, 0.15)	0.35 (0.45, 0.47, 0.18)	1.70 (1.6, 1.4, 1.7, 1.5, 1.9, 1.6)
10	0.001 (< 0.001, < 0.001, 0.002)	0.16 (0.14, 0.083, 0.27)	0.64 (0.72, 0.79, 0.40)	2.20 (2.1, 1.9, 2.5, 1.9, 2.6, 2.1)
14	0.001 (< 0.001, 0.001, 0.002)	0.27 (0.18, 0.33, 0.31)	0.70 ((0.54, 0.92, 0.54)	2.63 2.6, 2.6, 3.3, 2.9, 2.5, 1.9)
21	0.001 (< 0.001, 0.001, 0.001)	0.34 (0.32, 0.30, 0.41)	0.89 (0.81, 1.3, 0.57)	3.53 (4.6, 4.1, 4.7, 2.1, 3.1, 2.6)
28	0.001 (< 0.001, < 0.001, 0.001)	0.437 (0.39, 0.41, 0.51)	1.33 (1.4, 1.6, 1.0)	3.57 (4.3, 3.1, 3.7, 3.4, 4.0, 2.9)
35	0.0013 (< 0.001, < 0.001, 0.003)	0.460 (0.40, 0.49, 0.49)	1.37 (1.4, 1.6, 1.1)	3.72 (4.5, 2.6, 4.2, 3.9, 4.4, 2.7)
42	0.025 (0.002, 0.002, 0.07)	0.420 (0.40, 0.42, 0.44)	1.20 (1.1, 1.4, 1.1)	3.98 (4.4, 4.0, 4.4, 3.4, 3.8, 3.9)
56	0.003 (< 0.001, 0.002, 0.007)	0.493 (0.47, 0.51, 0.50)	1.57 (1.6, 1.8, 1.3)	5.02 (5.6, 4.6, 5.0, 5.1, 4.9, 5.0)
70	0.001 (< 0.001, < 0.001, 0.001)	0.58 (0.62, 0.56, 0.57)	1.80 (2.0, 1.8, 1.8)	5.45 (5.1, 5.8, 5.3, 5.8, 5.3, 5.4)
86	0.001 (0.001, 0.001, < 0.001)	0.64 (0.60, 0.75, 0.56)	1.53 (1.5, 1.6, 1.5)	5.47 96.2, 4.7, 5.0, 6.2, 4.8, 5.9)
90	0.001 (0.002, 0.001, < 0.001)	0.64 (0.77, 0.64, 0.51)	1.90 (2.2, 2.0, 1.5)	5.53 (6.5, 5.6, 5.4, 5.1, 4.4, 6.2)
Depuration Phase				
91	0.001 (0.001, 0.001, < 0.001)	–	–	5.13 (4.1, 4.2, 5.6, 5.4, 4.5, 6.9)
92	< 0.001	–	–	4.63 (4.7, 4.0, 5.2)
94	< 0.001	–	–	4.67 (3.9, 3.7, 6.4)
97	< 0.001	–	–	3.27 (3.2, 2.1, 4.5)

Study Day	Mean residues for flufenoxuron (mg/L)			
	Group A [a] control	Group B [a] 1.75 mg/kg diet	Group C [a] 5.25 mg/kg diet	Group D [b] 17.5 mg/kg diet
101	0.002	–	–	2.60 (2.7, 1.7, 3.4)
106	< 0.001	–	–	2.07 (2.1, 1.1, 3.0)
112	< 0.001	–	–	1.43 (1.7, 0.59, 2.0)
118	< 0.001	–	–	1.20 (1.3, 0.69, 1.7)
124	< 0.001	–	–	0.95 (1.1, 0.45, 1.3)
130	< 0.001	–	–	0.92 8.84, 0.61, 1.3)

[a] Mean values of three animals
[b] Mean values of six animals, three animals during depuration phase

Pasteurised milk, cream, skimmed milk and acid whey were prepared from pooled control milk (group A) and from pooled milk from the high-dose group (D) at the end of the 90 day dosing period. The mean results of the analyses of those milk products for both treatment groups are summarised in Table 45.

Table 45 Mean residues of Flufenoxuron in milk products after 90 days of dosing.

Product	Mean residues of flufenoxuron in milk products [mg/L]	
	Group A (Control)	Group D (17.5 mg/kg diet)
Raw Milk	0.001	5.5
Pasteurized Milk	0.012	6.4
Cream	0.007	28
Skimmed Milk	< 0.001	0.18
Acid Whey	< 0.001	0.06

Analysis of milk obtained from the high dose group showed that pasteurization had no effect on the levels of flufenoxuron in milk. Residues in cream were concentrated by a factor of 1.5. In skimmed milk and acid whey, residues were reduced compared to the raw milk.

The mean residue levels and individual sample residues in tissues are summarized in Table 46 for each treatment group.

Table 46 Residues of Flufenoxuron in bovine tissues collected 90 days following the last administered dose

Tissue type	Residues of Flufenoxuron in tissues [mg/kg]				
	Group A [a] control	Group B [b] 1.75 mg/kg diet	Group C [b] 5.25 mg/kg diet	Group D [b] 17.5 mg/kg diet	Group D [b] day 40 depuration
Muscle	< 0.03 (< 0.03, < 0.03)	0.14 [0.08, 0.20 (0.14) 0.12, 0.08 (0.10) 0.28, 0.08 (0.18)]	0.66 [0.67, 0.49 (0.59) 0.24, 0.38 (0.31) 1.2, 0.91 (1.1)]	1.63 [1.7, 1.7 (1.7) 1.8, 1.9 (1.9) 1.4, 1.3 (1.4)]	0.25 [0.28, 0.39 (0.34) 0.03, 0.06 (0.04) 0.27, 0.48 (0.37)]
Liver	< 0.03 (< 0.03, < 0.03)	0.74 [0.70, 0.83 (0.77) 0.83, 0.79 (0.81) 0.68, 0.64 (0.66)]	2.17 [2.2, 2.3 (2.3) 1.8, 2.1 (2.0) 2.2, 2.3 (2.3)]	8.70 [9.0, 11.0 (9.8) 7.5, 7.6 (7.6) 8.3, 9.3 (8.8)]	0.92 [1.0, 1.4 (1.2) 0.23, 0.28 (0.25) 1.0, 1.6 (1.3)]

Tissue type	Residues of Flufenoxuron in tissues [mg/kg]				
	Group A [a] control	Group B [b] 1.75 mg/kg diet	Group C [b] 5.25 mg/kg diet	Group D [b] 17.5 mg/kg diet	Group D [b] day 40 depuration
Kidney	< 0.03 (< 0.03, < 0.03)	0.34 [0.40, 0.24 (0.32) 0.43, 0.44 (0.44) 0.31, 0.23 (0.27)]	1.60 [(1.8, 1.1 (1.4) 1.1, 1.0 (1.1) 2.7, 2.1 (2.4)]	4.30 [5.4, 3.0 (4.2) 7.2, 4.0 (5.6) 3.2, 2.9 (3.1)]	0.71 [1.5, 1.0 (1.3) 0.19, 0.14 (0.17) 0.92, 0.40 (0.66)]
Subcutaneous Fat	< 0.03 (< 0.03, < 0.03)	0.84 [1.1, 2.9 (2.0) 0.37, 0.42 (0.39) 0.16, 0.12 (0.14)]	9.27 [13, 13 (13) 3.6, 4.0 (3.8) 7.4, 15 (11)]	8.70 [5.1, 9.9 (7.5 18, 11 (15) 4.1, 3.1 (3.6)]	3.467 [6.9, 4.8 (5.9) 0.77, 0.42 (0.60) 2.0, 5.8 (3.9)]
Peritoneal Fat	0.04 (0.04, 0.04)	2.31 [3.4, 6.9 (5.2) 1.3, 0.86 (1.1) 0.69, 0.56 (0.62)]	17.27 [22, 20 (2.1) 6.4, 7.2, (6.8) 25, 23 (24)]	29.33 [44, 47 (45) 28, 27 (28) 14, 16 (15)]	7.63 [12, 12 (12) 2.6, 2.2, (2.4) 9.2, 7.7 (8.5)]

[a] Only one control animal was sacrificed at the end of the 90-day dosing period
[b] Mean of three animals; for each animal two separate analyses were conducted for each tissue

Laying hen

Seventy five white female Leghorn laying hens (three subgroups per control and treatment group, five hens per subgroup; the depuration group consisted of three subgroups of five hens/subgroup), aged 8–9 months and weighing 1303–1896 g, were dosed orally (gavage) once daily with flufenoxuron for 50 consecutive days at 1, 3 and 10 mg/kg feed, based on a daily consumption of 150 g/bird/day, equivalent to 0.15, 0.45 and 1.5 mg/kg bw/day. The average lay efficiency was 0.5 egg/hen/day.

Eggs were collected daily and separated into yolks and whites then pooled by subgroup (of five hens), resulting in three replicate daily samples per treatment group.

Fifteen animals from the top dose group and ten animals from the control group were monitored for flufenoxuron residues over a 40-day depuration phase. Eggs from these animals were sampled during the depuration period.

One day after the last day of dosing (day 40), the birds, with the exception of those of the depuration group, were sacrificed and samples of skin, muscle (breast, leg and thigh pooled), fat and liver (total organs) were taken separately for analysis and subdivided into two subsamples per subgroup.

The egg and tissue samples were analysed for residues of flufenoxuron using Analytical Method SAMS 492-1 and Analytical Method SAMS 457-2, respectively. The limit of quantitation for flufenoxuron is 0.25 mg/kg in egg yolk and 0.05 mg/kg in egg white and tissues based on acceptable concurrent recoveries. The liver samples were also analysed for the metabolite Reg. No. 4064702 using the HPLC/UV Analytical Method 01791.PCC with a limit of quantitation 0 0.03 mg/kg.

Egg white and yolk samples were analysed separately. Unless otherwise identified, in the majority of cases, no residues of flufenoxuron in egg white exceeded 0.05 mg/kg. The mean residue levels and range of residues in egg yolks are summarized in Table 47.

Table 47 Residues of Flufenoxuron in egg yolks.

Study Day	Mean (range) residues for flufenoxuron in egg yolks (mg/kg)			
	Group A (control)	Group B (1 mg/kg diet)	Group C (3 mg/kg diet)	Group D (10 mg/kg diet)
–3	< 0.25	< 0.25	< 0.25	< 0.25
–1	< 0.25	< 0.25	< 0.25	< 0.25
1	< 0.25	< 0.25	< 0.25	< 0.25
2	< 0.25	< 0.25	0.28(< 0.25–0.30)	0.40 (0.27–0.47)
4	0.27	< 0.25	0.63 (0.44–1.0)	1.87 (1.25–2.30)

Study Day	Mean (range) residues for flufenoxuron in egg yolks (mg/kg)			
	Group A (control)	Group B (1 mg/kg diet)	Group C (3 mg/kg diet)	Group D (10 mg/kg diet)
7	< 0.25	0.54 (0.45–0.70)	2.07 (1.74–2.30)	5.35 (4.07–6.99)
14	< 0.25	1.32 (1.02–1.70) [a]	4.02 (3.18–4.83)	10.23 (7.82–12.61)
21	< 0.25	2.08 (1.65–2.66)	4.92 (3.34–5.76)	15.43 (12.65–20.80)
28	0.47 (< 0.25–0.88)	2.14 (1.78–2.36)	4.70 (4.53–5.58)	17.18 (13.05–20.22)
35	0.49 (< 0.25–0.89)	2.26 (1.37–3.19)	6.22 (5.45–7.37)	19.56 (15.39–26.42)
42	0.62 (< 0.25–1.64)	2.68 (2.46–2.84)	6.06 (4.11–6.96)	25.19 (23.17–28.02)
50	0.25 (< 0.25–0.27)	3.09 (2.57–3.81)	8.01 (7.23–8.58)	28.03 (22.62–31.78)
Depuration phase				
51	0.34 (< 0.25–0.43) [b]	–	–	32.53 (24.52–39.55) [c]
52	< 0.25 [b]	–	–	30.74 (17.31–40.76) [c]
54	< 0.25 [b]	–	–	37.73 (27.21–46.64) [c]
57	< 0.25 [b]	–	–	18.45 (14.94–20.78) [c]
61	0.35(< 0.25–0.45) [b]	–	–	13.54 (6.74–19.24) [c]
66	< 0.25 [b]	–	–	10.48 (9.48–11.54) [c]
72	< 0.25 [b]	–	–	9.46 (5.34–11.66) [c]
78	< 0.25 [b]	–	–	4.57 (3.01–5.67) [c]
84	< 0.25 [b]	–	–	2.73 (1.90–3.59) [c]
90	< 0.25 [b]	–	–	2.27 (2.07–2.47) [c]

[a] The sample of Group B collected on Day 14 was the only egg sample in which Flufenoxuron was also detected in egg white (group mean residue of 0.13 mg/kg, but detected only in one out of three subgroups (subgroup B2)); in each other egg white sample analysed (Day –3 to Day 50), the Flufenoxuron concentration was below 0.05 mg/kg

[b] During the depuration period, only the eggs of one control subgroup (5 hens) were analysed

[c] During the depuration period, only the eggs of 15 hens at the highest dose level were analysed

The mean and range of residue concentrations of flufenoxuron in hen tissues are listed in Table 48.

Table 48 Residues of Flufenoxuron in tissues

Tissue type	Mean (range) residues of Flufenoxuron in tissues [mg/kg]				
	Group A	Group B (1 mg/kg diet)	Group C (3 mg/kg diet)	Group D (10 mg/kg diet)	Group D Day 40 depuration
Liver	0.09	0.49 (0.31–0.59)	2.30 (0.17–3.89)	2.94 (1.20–4.28)	0.99 (0.48–1.85)
Muscle	0.63 (0.42–0.85)	0.19 (0.16–0.25)	0.69(0.52–0.85)	2.29 (1.92–2.50)	0.33 (0.15–0.53)
Skin	< 0.05	2.02 (1.56–2.67)	6.39 (5.90–7.23)	21.58 (13.24–26.21)	2.94(1.83–3.84)
Fat	0.27 (0.25–0.29)	5.57 (5.49–5.76)	16.9 (15.14–19.22)	69.4 (59.04–77.40)	13.7 (7.95–19.56)

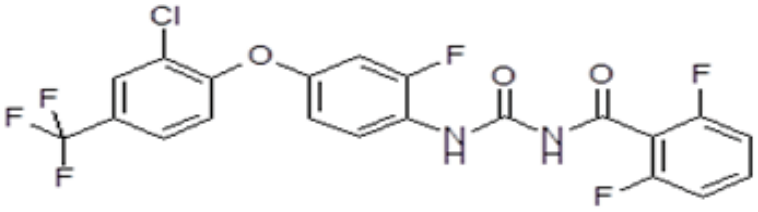
Table 49 Residues of Reg. No. 4064702 in liver

Mean (range) residues of Reg. No. 4064702 in Liver [mg/kg]				
Group A (Control)	Group B (1 mg/kg diet)	Group C (3 mg/kg diet)	Group D (10 mg/kg diet)	Group D Day 40 depuration
< 0.03	0.04 (< 0.02–0.04)	0.18 (0.054–0.37)	0.20 (0.10–0.36)	0.03 (0.028–0.036)

APPRAISAL

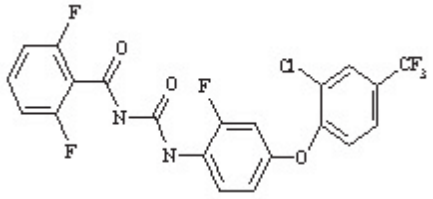
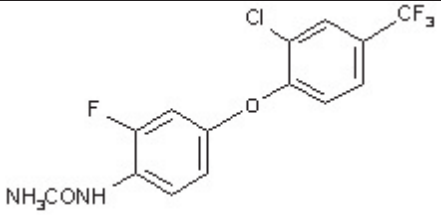
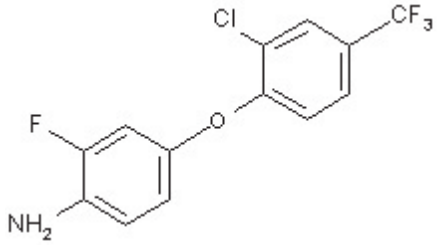
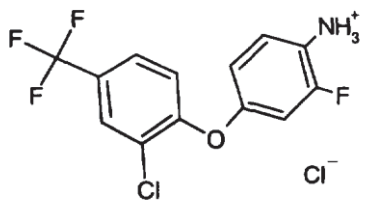
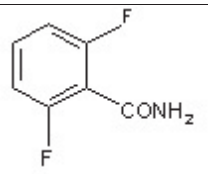
Flufenoxuron is a benzylurea insect growth regulator used to kill mites and insects, through interference with chitin production during cuticle development in mite and insect juvenile stages, on various orchard crops, fruiting vegetables and tea. It was considered for the first time by the 2014 JMPR for toxicology and residues.

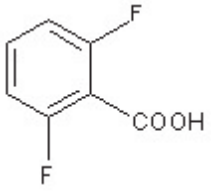
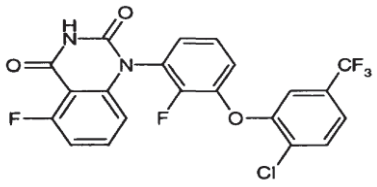
The Meeting received information on physical chemical properties, livestock and plant metabolism, environmental fate, analytical methods, storage stability, supervised residue trials, use patterns, processing and livestock feeding.



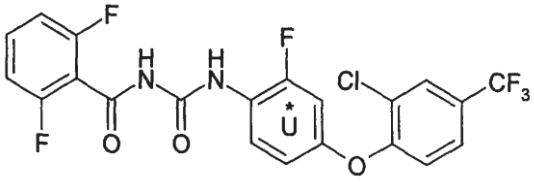
The IUPAC name of flufenoxuron is N-{4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl}-N'-(2,6-difluorobenzoyl)urea and the CA name is N-[[[4-[2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl]amino]carbonyl]-2,6-difluorobenzamide.

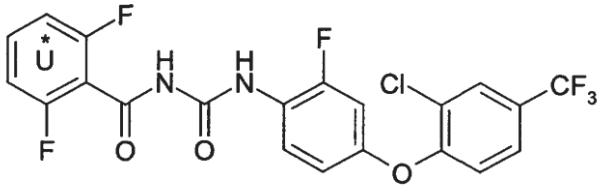
Common chemical names, code names and structures of the parent and metabolites are captured below:

Code	Structure	Occurrence
Flufenoxuron WL 115110		Rat Lactating goat Laying hen Grape Apple Tomato Chinese cabbage Soil Hydrolysis study
Reg. No. 4064702		Rat Laying hen Soil Hydrolysis study
Reg. No. 241208		Rat Laying hen Hydrolysis study
Reg. No. 4064703 (chloride salt of Reg. No. 241208)		Hydrolysis study
Reg. No. 102719		Rat Hydrolysis study

Code	Structure	Occurrence
Reg. No. 206925		Rat Hydrolysis study
Reg. No. 4964847		Hydrolysis study

Flufenoxuron uniformly labelled in either the fluoroaniline or difluoroamide rings was used in the metabolism and environmental fate studies.





Fluoroaniline U-^{14}C Difluoroamide U-^{14}C

Animal metabolism

Information was available on the metabolism of flufenoxuron in laboratory animals, lactating goats and laying hens.

Metabolism studies in rats demonstrated that unchanged flufenoxuron accounted for the majority of the total applied radioactivity (TAR) in faeces, with minor metabolites (less than 1% of the TAR) identified as 2-amino-5-(2-chloro-α,α,α-trifluoro-p-tolyoxy)-3-fluorophenol (Reg. No. 4110959), Reg. No. 4064702, Reg. No 241208, Reg. No 102719 and Reg. No. 206925. For organs and tissues, parent flufenoxuron was the main component observed.

In the lactating goat metabolism study, one goat received four daily doses of 2-fluoroaniline-[U-^{14}C]-ring-labelled flufenoxuron at a rate equivalent to 10 ppm in the diet (10 mg/day). The animal was sacrificed 24 hours after administration of the last dose. While the majority of the radioactivity was excreted via the faeces (18% of the TAR) and urine (2.5% of the TAR), milk and tissues accounted for ≤ 10% of the TAR. Total recovered radioactivity was low (33%). No explanation for the low recovery was evident.

The total radioactive residues (TRRs) were highest in fat (1.6 mg eq/kg), followed by liver (0.37 mg eq/kg), kidney (0.13 mg eq/kg) and muscle (0.076 to 0.1 mg eq/kg). Milk residues peaked on day 4 (average of 0.27 mg eq/L) with the highest concentrations of radioactivity detected in the cream fraction (accounting for 82–93% of the TRR in whole milk) and the lowest found in whey (1.3–5.7% of the TRR). Following solvent extraction, residue extractabilities were 66–100%.In milk

and all tissues sampled, the flufenoxuron molecule remained intact with no other metabolites being detected.

Two studies on metabolism in laying hens were available. In the first study, the laying hens received 14 daily doses of flufenoxuron, uniformly labelled in the difluoroamide or fluoroaniline rings, at 13–14 ppm in the feed. The animals were sacrificed approximately 23 h after the last dose. Excreta accounted for 72–78% of the TAR. No plateau was reached in eggs during the dosing period (14 days); however, the radioactivity in eggs and tissues amounted to 1.0–1.3% and 2.6–3.6% of the TAR, respectively. Among all the tissues analysed, radioactive residues were highest in fat (5.0–5.3 mg eq/kg) followed by liver (0.6–1.1 mg eq/kg) and muscle (0.3–0.4 mg eq/kg). The total recovery of radioactivity was 82% and 77% in the groups administered the difluoroamide- and fluoroaniline-labelled flufenoxuron, respectively.

Solvent extraction released 91–102% and 88–99% of the TRRs for the difluoroamide- and fluoroaniline-label, respectively. While the lowest extractability occurred in the liver of the fluoroaniline-labelled study (88% of the TRR), microwave extraction of the liver post-extraction solid (PES) sample released another 8% of the TRR. For the difluoroamide-label, the parent was the only analyte identified in eggs, muscle, fat and liver ranging from 0.28 mg eq/kg (86.5% of the TRR, muscle) to 4.6 mg eq/kg (91.4%, fat).

For the fluoroaniline-label, the parent compound accounted for the majority of the TRRs (70–91%) in the eggs, muscle, fat and liver. The lowest level of parent was found in muscle (0.30 mg eq/kg) with the highest observed in fat (4.8 mg eq/kg). In eggs and liver, Reg. No. 4064702 was present at 0.10 mg eq/kg and 0.13 mg eq/kg (12.0% and 12.6% of the TRR, respectively) while in muscle and fat, Reg. No. 4064702 was a minor metabolite amounting to 0.02 mg eq/kg and 0.05 mg/kg, respectively (5.5% and 1.0% of the TRR). The formate derivative of Reg. No. 241208 was released from the PES of liver after microwave treatment in the presence of formic acid/acetonitrile. The radioactivity associated with this derivative amounted to 0.04 mg eq/kg (3.3% TRR). The Meeting could not confirm whether the metabolite Reg. No. 241208 is an actual in-vivo metabolite or an artefact formed during microwave treatment.

In the second study, laying hens received seven consecutive daily doses of flufenoxuron uniformly labelled in the fluoroaniline ring at a rate equivalent to 10 ppm in the diet. Hens were sacrificed 22 hours following administration of the last dose. To investigate the depuration behaviour of flufenoxuron, four groups of three laying hens each were sacrificed at 2, 9, 16, and 34 days after the last administration.

On average, 26% of the TAR was excreta-related with eggs, sampled from 0–166 h after the first administration, accounting for 5% of the TAR. At sacrifice, the highest amount of radioactive residues was detected in fat (47% of the TAR), followed by skin (12% of the TAR), muscle (4% of the TAR), liver (2% of the TAR), kidney (0.3% of the TAR), heart and gizzard (combined 0.2% TAR). The recovery of radioactivity amounted to 96% of the TAR.

Solvent extraction (including incubation of liver and kidney samples at 37 °C) released 91–102% of the TRRs). The parent compound was the predominant analyte detected in yolks, liver, kidney, muscle, gizzard and heart while it was the only compound detected in fat and skin. The metabolite Reg. No. 4064702 was detected in yolks, liver, kidney, muscle, gizzard, and heart at 6–22% of the TRR, while the minor metabolite Reg. No. 241208 was only detected in liver and kidney at ≤ 4% of the TRR, the only matrices that were incubated for 16 hours at 37 °C in 0.07M phosphate buffer at pH 7.5 prior to extraction

In the depuration study, radioactivity in egg yolks decreased steadily from a mean of 0.02 mg eq./kg, 2 days after cessation of dosing to 0.006 mg eq.kg on depuration day 34. Similarly, radioactivity in muscle decreased from 0.28 mg eg/kg to 0.06 mg eq/kg, during this same interval In kidney and liver, the decrease in radioactivity was more prominent from day 16 to day 34 of the depuration phase (kidney; 0.48 mg eq/kg to 0.17 mg eq/kg and liver; 0.89 mg eq/kg to 0.42 mg eq/kg) yet in fat, the decrease in radioactivity occurred most rapidly from day 2 to day 9 (13.18 mg eq/kg to 6.00 mg eq/kg) and from day 16 to day 34 (4.6 mg eq/kg to 1.97 mg eq/kg). These results

demonstrate that radioactive residues are not retained in eggs, organs and tissues after cessation of dosing.

In both laying hen studies, the metabolic pattern was comparable with unchanged flufenoxuron accounting for the majority of the radioactivity, representing ≥ 60% of the TRRs in eggs and tissues. The minor metabolites Reg. No. 4064702 (eggs and tissues) and Reg. No. 241208 (liver and kidney), resulting from the cleavage of the benzoyl urea bond, were also observed to a limited extent (≤ 12% of the TRRs; except in the kidney where Reg. No. 4064702 represented 22% of the TRRs).

The Meeting concluded that in the lactating goat metabolism study, the parent flufenoxuron remained intact and was the only residue identified in milk and all tissues. In the laying hen metabolism studies, while flufenoxuron was the predominant residue in eggs and tissues, cleavage of the benzoyl urea bond was observed to a limited extent resulting in the formation of the metabolites Reg. No. 4064702 (eggs and tissues) and Reg. No. 241208 (liver and kidney).which were also identified in the rats.

Plant metabolism

The Meeting received metabolism studies for flufenoxuron following foliar applications of either [difluorobenzamide-U-^{14}C]- or 2-fluoroaniline-[U-^{14}C]-ring-flufenoxuron to grape, apple, tomato and Chinese cabbage.

Two foliar sprays were made to grape vines, grown outdoor and protected with plastic covers after application, during fruit development; at a rate of 0.04 kg ai/ha/application, with a 40-day retreatment interval, resulting in a total rate of 0.08 kg ai/ha. Immature leaves were collected at 15 DAT (days after last treatment) while mature leaves, stalks and fruit (from grape clusters) were harvested 28–29 DAT. TRRs in leaves declined from 2.3–2.7 mg eq/kg at 15 DAT to 1.4–1.8 mg eq/kg at 29 DAT. TRRs in mature fruit and stalks were 0.012–0.014 mg eq/kg and 0.11–0.16 mg eq/kg, respectively. Solvent extraction released approximately 95–97% of the TRR (0.012–2.6 mg eq/kg) from the grape matrices. Flufenoxuron was the only compound identified in all fruit, leaf and stalk samples (50–97% of the TRR; 0.007–2.2 mg eq/kg). Polar unknowns comprised up to 40–46% of the TRR in mature grape samples (0.005–0.006 mg eq/kg) with unextracted residues in all leaf, fruit and stalk samples accounting for ≤ 5% of the TRR (< 0.11 mg eq/kg).

Ten apple trees, maintained in glasshouses, were sprayed with flufenoxuron, uniformly labelled in the fluoroaniline ring. A single application of the dispersible concentrate was made to trees, during fruit development, at a rate of 0.01 kg ai/hL. Samples of immature fruit were harvested 0 days (4 h post-treatment) and 46 days after treatment (DAT), and mature fruit samples were collected at 99 DAT. TRRs in immature fruit were 2.6 mg eq/kg (0 DAT) and declined to 0.16 mg eq/kg (46 DAT) and 0.06 mg eq/kg (99 DAT). The radioactivity in the combined acetonitrile and hexane surface washes decreased with increasing DAT, from 96% of the TRRs at 0 DAT to 77% of the TRRs at 99 DAT, with a corresponding increase in TRRs in fruit extracts (3.7% TRR at 0 DAT to 23% of the TRRs at 99 DAT), demonstrating limited translocation. The parent flufenoxuron accounted for the majority of the TRRs in surface washes (74–93%; 0.043–2.4 mg eq/kg) and in fruit extracts (3–16% of the TRRs; (0.01–0.08 mg eq/kg).

A single broadcast foliar application of 2-fluoroaniline-[U-^{14}C]-ring-flufenoxuron, formulated as an emulsifiable concentrate, was made to tomato plants, maintained outdoor, during fruit development at a rate of 0.125 kg ai/ha. Tomato fruit was harvested at 0 and 28 DAT. TRRs in/on tomato fruit declined from 0.38 mg eq/kg on day 0, to 0.2 mg eq/kg by day 28. The total extracted residues (ACN:water surface washes and fruit extracts) from 0 DAT to 28 DAT, accounted for 94–99% of the TRR (0.16–0.38 mg eq/kg), mainly from the surface wash (≥ 94% of the TRRs). Flufenoxuron was the only identified residue in the mature tomato sample (91% of the TRRs).

2-Fluoroaniline-[U-^{14}C]-ring-flufenoxuron, formulated as an emulsifiable concentrate, was applied once to Chinese cabbage plants, grown outdoor, during leaf development, as a foliar application, at a rate equivalent to 0.10 kg ai/ha. Cabbage plants were harvested at 0 and 28 DAT.

TRRs in/on cabbage wrapper leaves declined from 6.3 mg eq/kg on day 0 to 0.35 mg eq/kg by day 28. At 0 DAT, the surface wash represented the majority of the extracted residues (84% of the TRRs; 5.3 mg eq/kg) while at the 28 DAT, the leaf extracts accounted for a greater fraction of the extractable radioactivity (76% of the TRRs; 0.27 mg eq/kg). The parent flufenoxuron was the only identified residue in mature cabbage leaves (93% of the TRRs).

The Meeting concluded that the metabolism of flufenoxuron in grape, apple, tomato and Chinese cabbage is consistent among all crops, where parent flufenoxuron remained intact. No other metabolites were identified and no other residues were characterized (other than polar unknowns). The Meeting agreed that the majority of radioactivity remained on the leaves or surface of the fruit, with limited translocation.

Environmental fate in soil

The Meeting received information on aerobic degradation in soil.

In these studies, the fluoroaniline-specific metabolite, Reg. No. 4064702, was the only metabolite identified, reaching a maximum concentration after 30 days of incubation (4.1–8.3% TAR). The predominant residue, flufenoxuron, decreased to 45.8–51.0% TAR in the soil after 119 days, resulting in a calculated DT_{50} for flufenoxuron of 115–122 days. Considering the persistence of flufenoxuron, it is desirable that confined rotational crop and field accumulation studies be submitted.

Methods of residue analysis

The Meeting received analytical methods for the analysis of flufenoxuron in plant and animal commodities. The basic principle for plant commodities employs extraction by homogenisation with dichloromethane, methanol/water/HCl or acetone followed by partitioning with water/cyclohexane. For animal matrices, flufenoxuron residues are extracted by homogenization with various non-polar organic solvents followed by liquid partitioning and/or clean-up by normal-phase or reverse-phase HPLC prior to analysis. Residues of flufenoxuron are measured by HPLC-MS/MS with two specific mass transitions or with HPLC-UV at 254–260 nm. The applicability of the proposed enforcement methods was confirmed in various independent laboratories where parent flufenoxuron was analysed with validated LOQs of 0.05 mg/kg for plant and animal commodities and eggs, and 0.01 mg/kg for milk.

The multiresidue method DFG S-19 was tested, for the analysis of flufenoxuron in animal matrices only, and found to be unsuitable.

A number of scientific papers report the validation of the QuEChERS multi-residue method using GC-MS/MS for flufenoxuron in various plant commodities.

The Meeting concluded that the available enforcement analytical methods are suitable for determining residues of flufenoxuron in plant and animal commodities with LOQs, ranging from 0.01–0.05 mg/kg depending on the matrix.

Stability of residues in stored analytical samples

Based on the storage stability data submitted, the Meeting concluded that no significant dissipation of flufenoxuron residues was observed in cottonseed, orange, grape, and apple after 36 months of storage, in lettuce after 27 months and in watermelon (pulp and peel) after 26 months.

The Meeting agreed that no degradation of flufenoxuron residues was observed in animal matrices stored for up to 53 months of storage, except egg whites, where flufenoxuron residues were determined to be stable for up to 4 months.

Definition of the Residue

In the lactating goat metabolism study, flufenoxuron was the only residue identified in tissues and milk with no other metabolites detected. Similarly, in the laying hen metabolism studies, flufenoxuron

accounted for the majority of the radioactivity in eggs, muscle, fat, liver and kidney (60–104% of the TRRs).

Therefore, the Meeting recommends the residue definition for compliance with MRL for animal commodities as flufenoxuron.

The Log K_{ow} of flufenoxuron is 4. In the goat metabolism study, highest levels of the parent compound were observed in fat and cream, while in the laying hen metabolism studies, the highest concentrations of flufenoxuron were observed in the fat (≤ 98% of the TRRs). These findings were supported by the livestock feeding studies, where the average ratio for cream/skim milk was ≥ 155 and ≥ 112 for egg yolks/egg whites. Further to this, residues in fat were 24–30-fold higher than those in muscle.

In light of this, the Meeting concluded that the residue is fat soluble.

The metabolite Reg. No. 4064702 was also identified in laying hen muscle, fat, liver, kidney and eggs (1–22% of the TRRs) with the highest levels observed in liver and kidney. The minor metabolite Reg. No. 241208 was also observed but only in liver and kidney (2.5–3.7% of the TRRs) which were the only matrices that were subject to microwave extraction (liver only) or incubation at 37 °C in 0.07M phosphate buffer at pH 7.5 prior to extraction (liver and kidney), and hence considered a potential artefact of the analytical procedure.

The toxicity of the minor metabolite Reg. No. 241208, found in laying hen matrices, was considered to be covered by toxicity studies on flufenoxuron since this metabolite was seen in the rat. The metabolite Reg. No. 4064702, also observed in eggs and tissues of laying hens, and observed in the rat, was determined to be more acutely toxic than the parent flufenoxuron based on the LD_{50}. However, according to the poultry feeding study, residues of this metabolite in liver are not expected to exceed 0.04 mg/kg at the lowest feeding level of 1 ppm. Hence, as there are no poultry feed items derived from the proposed crops, the dietary exposure to this metabolite from poultry matrices is unlikely.

The Meeting recommends the residue for dietary intake for animal commodities as parent only.

The fate of flufenoxuron in plants was investigated following foliar application to tomato, apple, grape and Chinese cabbage. In all plant commodities tested, flufenoxuron was the predominant residue accounting for > 90% of the TRR, with the exception of grape, where flufenoxuron accounted for 50% of the TRR. No other metabolites were identified and no other residues were characterized (other than polar unknowns).

According to the hydrolysis study, simulating typical processing conditions (pH 4, 5 and 6 with 90 °C, 100 °C and 120 °C for 20, 60 and 20 minutes), flufenoxuron was degraded to various metabolites including: Reg. No. 102719 (8–32%), Reg. No. 4064702 (4%) and Reg. No. 4964847 (4–9%). All metabolites, except Reg. No. 4064702 and Reg. No. 4964847 are considered to be covered by toxicity studies on flufenoxuron, since they were seen in the rat. The absorption, distribution, metabolism and excretion studies in rat demonstrated that Reg. No. 4064702 was more acutely toxic than the parent flufenoxuron. Conversely, no toxicity information is available on metabolite Reg. No. 4964847, Reg. No. 4064702. Nevertheless, in the tomato processing study where these metabolites were measured in juice, purée and canned tomatoes, none were detected (< 0.01 mg/kg)

The Meeting recommended the following residue definition for flufenoxuron:

Definition of the residue for compliance with MRL and for estimation of dietary intake for plants and animal commodities: *flufenoxuron*

The Meeting considers the residue fat soluble.

Results of supervised residue trials on crops

The Meeting received supervised residue trials from Brazil, Europe and South Africa where flufenoxuron was applied to oranges, apples, pears, melons and tomatoes and Japanese trials on tea.

Oranges

The critical GAP in Brazil for flufenoxuron on oranges is up to two foliar applications of 0.005 kg ai/hL, with a re-treatment interval of 30 days and a PHI of 15 days. Sixteen supervised field trials were conducted in Greece, Italy, South Africa and Brazil.

Four of the trials were conducted in Brazil according to the critical GAP. Residues in whole oranges at the 15-day PHI were: 0.09, 0.11, 0.13 and 0.16 mg/kg.

Five trials in Brazil were conducted at 2× 0.002–0.003 kg ai/hL with a PHI of 15 days, representing 0.4–0.6× the critical GAP in Brazil. The residues in whole fruit were 0.03, 0.05, 0.07, 0.08 and 0.10 mg/kg. The Meeting agreed to use the proportionality approach to scale the residues at the 15-day PHI according to an application rate of 0.005 kg ai/hL. The rank order of scaled residues in whole fruit was (n = 5): 0.08 (2), 0.13 (2), and 0.17 mg/kg.

When combining all the residue data, residues in whole oranges were 0.08 (2), 0.09, 0.11, 0.13 (3), 0.16 and 0.17 mg/kg and residues in pulp were 0.03, 0.04, 0.05 (3), 0.06, 0.08 (2) and 0.10 mg/kg.

The Meeting estimated a maximum residue level of 0.4 mg/kg, and a median residue of 0.13 mg/kg for residues of flufenoxuron in whole oranges. For orange pulp, the Meeting estimated an STMR of 0.05 mg/kg.

Apples

The Brazil critical GAP for flufenoxuron on apples is a single foliar application at 0.01 kg ai/hL and a PHI of 35 days.

Three trials on apples were available from Chile where trees were treated at 0.015–0.02 kg ai/hL with PHIs of 35–36 days, representing 1.5–2× the critical GAP in Brazil. The residues in the fruit were 0.17, 0.43 and 0.52 mg/kg. The Meeting agreed to use the proportionality approach to scale the residues at the PHIs of 35–36 days according to the application rate of 0.01 kg ai/hL. The ranked order of the scaled residues were: 0.08, 0.22 and 0.35 mg/kg (n=3).

In two trials conducted in Chile in accordance with Brazilian GAP, flufenoxuron residues were 0.07 and 0.45 mg/kg.

The Meeting concluded that the number of trials available was insufficient to estimate a maximum residue level for residues of flufenoxuron in apples.

Melons

There is no GAP in Brazil for flufenoxuron on melons; therefore, the Meeting could not recommend a maximum residue level.

Tomatoes

There is no GAP in Brazil for flufenoxuron on tomatoes; therefore, the Meeting could not recommend a maximum residue level.

Tea

The critical GAP for flufenoxuron in Japan for tea is up to two foliar applications of 0.025 kg ai/hL at a re-treatment interval of 7–14 days and a PHI of 7 days.

In seven of the eleven trials conducted in Japan and matching the critical GAP, residue levels in tea (green) were: 2.37, 2.48, 3.95, 4.58, 6.02, 6.23 and 11.8 mg/kg.

The Meeting estimated a maximum residue level of 20 mg/kg and a STMR of 4.58 mg/kg for residues of flufenoxuron in tea, green, black (black, fermented and dried).

Fate of residues during processing

Nature of residues

The Meeting received information on the hydrolysis of flufenoxuron uniformly labelled in the fluoroaniline and difluoroamide rings where typical processing conditions were simulated (pH 4,5 and 6 with 90 °C, 100 °C and 120 °C for 20, 60 and 20 minutes).

In duplicate samples of sterile buffer solution flufenoxuron (accounting for 63–93% of the TAR) was seen to hydrolyse to various metabolites, however, none accounted for greater than 10%of the TAR, with the exception of Reg. No. 102719, present at 32% of the TAR, following hydrolysis conditions simulating baking, boiling and brewing procedures.

Level of residues

The Meeting also received information on the fate of flufenoxuron residues during the processing of the raw agricultural commodities like tomato to juice, pomace, puree and canned tomatoes and tea to infusion. While the magnitude of the residues of Reg. No. 102719in tea infusion was not elucidated, in the tomato processing study, the residues of flufenoxuron metabolites, including Reg. No. 102719, Reg. No. 4064702 and Reg. No. 4964847 in all processed tomato commodities were below the LOQ (0.01 mg/kg). However, in the absence of a critical GAP in Brazil for flufenoxuron on tomatoes, the tomato processing study was not relied upon to derive processing factors, STMR-P values and to estimate maximum residue levels for tomato processed commodities.

The processing factor obtained in the tea processing study and the estimated STMR-P value for the dietary intake calculation is summarized below:

Raw agricultural commodity	STMR, mg/kg	Processed commodity (food)	Processing factor	STMR-P (mg/kg)
Tea (green)	6.02	Infusion	0.0065 (median)	0.04

Residues in animal commodities

Farm animal feeding studies

The Meeting received information on the residue levels arising in animal tissues and milk when dairy cows were fed flufenoxuron for 90 days at levels equivalent of 1.75, 5.25 and 17.5 ppm in the diet. Three animals from the highest dose level group were monitored for flufenoxuron residues over a 40-day depuration phase.

At the lowest dose tested, flufenoxuron residues in milk increased steadily over the 90-day period, from 0.0243 mg/kg on day 2 to 0.64 mg/kg on day 90, however, in the mid and high dose groups, residues seemed to plateau on day 56 (at 1.6 mg/kg) and day 70 (at 5.5 mg/kg), respectively. Analysis of milk obtained from the high dose group showed that pasteurization had no effect on the levels of flufenoxuron in milk. Residues in cream were concentrated by a factor of 1.5. In skimmed milk and acid whey, residues were lower than those of raw milk.

In all tissues tested, except subcutaneous fat, residues of flufenoxuron were dose dependant, increasing with increasing dose. In subcutaneous fat, residues were 0.8 mg/kg, 9.3 mg/kg and 8.7 mg/kg, in the low, mid and high dose groups, respectively.

The residue depuration study demonstrated that flufenoxuron residues in milk decreased slowly within the 40 days of cessation of dosing, from 5.1 mg/kg on day 91 to 0.9 mg/kg on day 130. In tissues, flufenoxuron residues decreased on average by 80% by day 130.

The Meeting also received information on the residues in tissues and eggs of laying hens when dosed with flufenoxuron for 50 days at levels equivalent to 1, 3, 10 ppm in the diet. Fifteen animals from the top dose group were monitored for flufenoxuron residues over a 40-day depuration phase.

At all feeding levels, no residues of flufenoxuron in egg white exceeded 0.05 mg/kg. However, residues in egg yolks did not reach a plateau but rather increased steadily over the 50-day period.

Residues of flufenoxuron in liver, muscle, skin and fat increased with increasing feeding level.

During the depuration study, flufenoxuron residues in egg yolks decreased more rapidly than in cattle milk over the same duration, from 32.5 mg/kg on day 51 to 2.3 mg/kg on day 90.

Farm animal dietary burden

As there is no information on citrus dry pulp, the only potential cattle feed item derived from the proposed crops and there are no poultry feed items, the Meeting did not calculate farm animal dietary burdens.

Therefore, the Meeting estimated maximum residue levels of 0.05* mg/kg for flufenoxuron in meat (from mammals other than marine mammals), edible offal (mammalian), mammalian fat (except milk fats) and 0.01* mg/kg for milks. STMRs and HRs for dietary intake estimation are 0 mg/kg for meat (from mammals other than marine mammals), edible offal (mammalian), mammalian fat (except milk fats) and milks.

The Meeting did not estimate maximum residue levels, STMRs or HRs for poultry matrices.

The residue in animal commodities is considered fat soluble.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI assessment.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake, animal and plant commodities): *flufenoxuron*

The residue is fat soluble.

CCN	Commodity Name	MRL mg/kg	STMR or STMR-P mg/kg	HR or HR-P mg/kg
FC 0004	Oranges, Sweet, Sour	0.4	0.13	–
	Orange pulp	–	0.05	–
DT 1114	Tea, Green, Black (black, fermented and dried)	20	4.58	–
	Tea infusion	–	0.04	–
MO 0105	Edible offal (mammalian)	0.05*	0	–
MM0095	Meat (from mammals other than marine mammals)	0.05*	0	–
MF 0100	Mammalian fats (except milk fats)	0.05*	0	–
ML 0106	Milks	0.01*	0	–

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intake (IEDI) for flufenoxuron was calculated based on the recommendation for STMRs for raw and processed commodities (tea infusion) in combination with consumption data for corresponding food commodities. These results are shown in Annexe 3.

The IEDI of the 17 GEMS/Food cluster diets, based on the estimated STMRs represented 0% of the maximum ADI of 0.04 mg/kg bw, expressed as flufenoxuron. The Meeting concluded that the

long-term intake of flufenoxuron residues from uses considered by the Meeting is unlikely to present a public health concern.

Short-term intake

No ARfD was considered necessary. The Meeting concluded that the short-term intake of flufenoxuron residues from uses considered by the Meeting is unlikely to present a public health concern.

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